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Methanolysis of Myrtenyl Chloride

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METHANOLYSIS OF MYRTENYL CHLORIDE

A thesis submitted by

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SUMMARY

The mechanism of reaction of myrtenyl chloride in methanol was studied. The effects of a neutral salt (lithium perchlorate), and of two nucleophiles (sodium methoxide and potassium acetate), on products and kinetics were evaluated. Methanolysis of trans-pinocarvyl chloride was also investigated briefly.

Reaction products were analyzed by gas-liquid chromatography and nuclear magnetic resonance spectroscopy. Reactant and product concentration analysis for kinetics was also done by gas-liquid chromatography.

Under all conditions studied, substitution products quantitatively accounted for the starting chlorides, and no elimination products were found. The products obtained from myrtenyl chloride in 2,6-dimethylpyridine-buffered methanol at 35.0°C. were 90% myrtenyl and 10% trans-pinocarvyl methyl ethers. Under the same conditions trans-pinocarvyl chloride gave 68% myrtenyl and 32% trans-pinocarvyl methyl ethers. Neither gave any cis-pinocarvyl methyl ether. Under these conditions the first-order methanolysis rate constants for myrtenyl and trans-pinocarvyl chlorides were 3.0- and 15.4 x 10^{-6} $sec.^{-1}$, respectively. The presence of 0.05M lithium perchlorate did not change the methanolysis product distribution. The first-order methanolysis rate constant for myrtenyl chloride was increased only slightly to 3.17 x 10^{-6} $sec.^{-1}$. The pseudo-first-order experimental rate constant for myrtenyl chloride increased linearly as initial sodium methoxide concentration was increased from 0.00 to 0.05M throughout a series of runs. Ionic strength was maintained constant by keeping the total salt concentration at 0.05M throughout the series with lithium perchlorate. The second-order rate constant for reaction of myrtenyl chloride with sodium methoxide was 75.9 x 10^{-6} M^{-1} $sec.^{-1}$. The proportion of myrtenyl methyl ether in the products also increased as initial sodium methoxide concentration was increased. The ratio of the second-order rate constant — concentration product to

the total observed (pseudo first-order) rate constant was used for the proportion of myrtenyl methyl ether which resulted from direct displacement of chloride by methoxide. Likewise, the ratio of the methanolysis rate constant to the total observed (pseudo first-order) rate constant was used for the proportion of myrtenyl methyl ether which resulted from methanolysis of myrtenyl chloride. These proportioning factors were used to calculate the mole percentage myrtenyl methyl ether in the products, as a function of initial methoxide concentration. The agreement between the calculated results and the experimentally determined percentage was excellent, verifying the hypothesis that myrtenyl chloride reacts with methoxide to give only myrtenyl methyl ether.

In the presence of 0.3M potassium acetate myrtenyl chloride gave 26% myrtenyl acetate, 66% myrtenyl, and 8% trans-pinocarvyl methyl ethers. No trans-pinocarvyl acetate was found. The percentage of myrtenyl acetate found was the same as the ratio of the second-order rate constant — concentration product to the observed experimental rate constant.

Methanolysis of myrtenyl chloride was concluded to proceed by an SN1 mechanism. The intermediate was concluded to be an intimate ion-pair because of the spread between the percentage of myrtenyl methyl ether from myrtenyl chloride and from trans-pinocarvyl chloride. Reactions of myrtenyl chloride with methoxide and with acetate were concluded to proceed by SN2 mechanisms which are concurrent and competitive with SN1 methanolysis. An alternate to the SN1 and SN2 mechanisms was recently proposed by Sneen and Larsen (5, 6). This mechanism proceeds by attack of both solvent and nucleophiles on an intimate ion-pair solvolysis intermediate. Sneen and Larsen have claimed that all nucleophilic substitutions at saturated carbon proceed by this mechanism. The results of this thesis indicate that not all nucleophilic substitutions at saturated carbon proceed by attack of nucleophiles on preformed ion-pairs.

INTRODUCTION

NUCLEOPHILIC SUBSTITUTION REACTIONS

Nucleophilic substitution at saturated carbon has been studied extensively for forty years. Two clearly distinct mechanisms, called SN1 and SN2, were proposed by Ingold and his coworkers (1) to explain the data known to them. The designation SN stands for substitution, nucleophilic. The numbers designate the molecularity of the rate-determining step. In the intervening years, the majority of nucleophilic-substitution-at-saturated-carbon reactions studied have been shown to follow one pathway or the other. A significant number of compounds appear to react by both mechanisms simultaneously when two nucleophiles are present. This is especially true if one nucleophile is a reactive part of the solvent, and the other is a strong Lewis base. Extensive reviews of theory and data are available (1-4).

An SN1 mechanism, as conceived by Ingold (1) is unimolecular because heterolysis of the C-X bond (to give R^+ and X^- from an initially neutral RX) is the slowest step. All the pertinent steps of the classic SN1 mechanism are shown in Scheme 1. A^- is a generalized nucleophilic anion and SOH is a generalized hydroxylic solvent.

Scheme 1

$$RX \underset{}{\overset{\text{slow}}{\rightleftharpoons}} R^+ + X^-$$

$$R^+ + A^- \xrightarrow{\text{fast}} RA$$

or

$$R^+ + HOS \xrightarrow{\text{fast}} ROSH^+$$

$$ROSH^+ \xrightarrow{\text{fast}} ROS + H^+$$

The other possibility suggested by Ingold and his coworkers (1), the SN2 mechanism, requires a nucleophile (which could also be the solvent) to attack the α-carbon on the side away from the leaving group, X. Scheme 2 shows this possibility for both anion and solvent attack. The rate-determining step is bimolecular.

Scheme 2

$$A^- + RX \xrightarrow{\text{slow}} AR + X^-$$

$$HOS + RX \xrightarrow{\text{slow}} HSOR^+ + X^-$$

$$HSOR^+ \xrightarrow{\text{fast}} SOR + H^+$$

THE ION-PAIR MECHANISM

A related, yet significantly different mechanism has recently been proposed by Sneen and Larsen (5-7). They envision an intimate ion-pair intermediate (R^+X^-). It would be in equilibrium with unionized RX, but it would not dissociate further to a solvent-separated ion-pair (8). The ion-pair intermediate would be attacked by solvent, HOS, and/or nucleophilic anions, A^-, to give products SOR and/or AR, as shown in Scheme 3. The reaction can be either bimolecular or unimolecular

Scheme 3

$$RX \underset{k_R}{\overset{k_F}{\rightleftharpoons}} R^+X^-$$

$$R^+X^- + HOS \xrightarrow{k_S} HSOR^+ + X^-$$

$$HSOR^+ \xrightarrow{\text{fast}} SOR + H^+$$

$$R^+X^- + A^- \xrightarrow{k_A} AR + X^-$$

depending on which step is rate-determining.

Kinetics is generally the best criterion for judging which mechanism a reaction follows. The major exception, however, is solvolysis. A unimolecular reaction should be first-order in RX and zero-order in A^-. A bimolecular reaction should be first-order in both RX and A^-. Experimentally, the pseudo-first-order rate constant for reaction of RX with both HOS and A^-, $\underline{\underline{k}}_{OBS}$, should be a linear function of initial A^- concentration (when it is present in sufficient excess over RX) for an SN2 mechanism. The rate constant, $\underline{\underline{k}}_{OBS}$, should not be affected any differently by A^- than by a nonnucleophilic salt for an SN1 mechanism. In the ion-pair mechanism the kinetics are not as simple. Sneen and Larsen (5) derive the following equation for $\underline{\underline{k}}_{OBS}$, the pseudo-first-order, experimental rate constant, where A is the initial concentration of A^- and the specific rate constants are shown in Scheme 3. In the absence of A^-, $\underline{\underline{k}}_{OBS}$ becomes

$$k_{OBS} = \frac{k_F(k_S + k_A A)}{k_R + k_S + k_A A} \qquad (1)$$

$$k_{NA} = \frac{k_F k_S}{k_R + k_S}. \qquad (2)$$

Dividing Equation (1) by Equation (2) and division of both numerator and denominator by $\underline{k}_S^2$ gives

$$\frac{k_{OBS}}{k_{NA}} = \frac{(x + 1)(1 + mA)}{x + 1 + mA} , \qquad (3)$$

where $\underline{m}$ is $\underline{k_A}/\underline{k_S}$, the ratio of RA to ROS product; and $\underline{x}$ is $\underline{k_R}/\underline{k_S}$, the ratio of recombination to solvolysis for the ion-pair intermediate. At the extremes, where $\underline{x} \rightarrow 0$ or ∞, Equation (3) reduces to an SN1 or SN2 rate equation, respectively. At intermediate $\underline{x}$ values (practically, $0.5 < \underline{x} < 10$), a plot of $\underline{k_{OBS}}/\underline{k_{NA}}$ vs. A should be concave downward.

APPLICATION TO ALLYLIC SYSTEMS

Application of these mechanisms to allylic compounds, AyX, requires further investigation of possible products. This is necessary because the π bond between the β- and γ-carbons of the allyl group can shift to the α- and β-carbons while the incoming nucleophile goes to the γ-carbon (Fig. 1).

$$\underset{\alpha}{X{-}CR_1R_2{-}}\underset{\beta}{CR_3}{=}\underset{\gamma}{CR_4R_5}$$

Figure 1. A Generalized Allylic Compound, Showing the α, β, and γ Carbons

De Wolfe and Young (9) have written an extensive review of the chemistry of allylic compounds.

An allylic halide or ester, AyX, could be attacked directly at the α-carbon by a nucleophile, A^- or HOS, to give the product AyA or AyOS by a classic SN2 mechanism as shown in Scheme 4.

Scheme 4

$$AyX + A^- \xrightarrow{\text{slow}} AyA + X^-$$

and/or

$$AyX + HOS \xrightarrow{slow} AyOSH^+ + X^-$$

$$AyOSH^+ \xrightarrow{fast} AyOS + H^+$$

The propensity of allylic compounds to give rearranged products, Ay'OS and Ay'A, as well as normal products, AyOS and AyA (9), cannot be accommodated by this mechanism. Thus, finding Ay'A from a reaction which is otherwise suspected of being bimolecular, because of kinetic dependency on A^-, is very good evidence of the SN2' mechanism (4). Scheme 5 shows this variation. Note that the α-carbon

Scheme 5

$$H_2C{=}CH{-}CHRX + A^- \longrightarrow AH_2C{-}CH{=}CHR + X^-$$

of the substrate has attached to it a group other than H. The only compounds which react by second-order kinetics and give a significant fraction of rearranged product have bulky groups on the α-carbon (4). Further, SN2' reactions generally occur with bulky neutral molecules or resonance stabilized anions (9). Compounds with electronegative α-substituents, such as 3,3-dichloropropene, react with ethoxide, phenoxide and thiophenoxide in ethanol by competitive SN2 and SN2' mechanisms (10).

The Allylic Ion-Pair Mechanism

A significantly different mechanism, which could be either uni- or bimolecular in the rate-determining step, is shown in Scheme 6. This is the ion-pair mechanism

Scheme 6

$$AyX \underset{k_R}{\overset{k_F}{\rightleftharpoons}} Ay^+X^-$$

$$Ay^+X^- + A^- \xrightarrow{k_A} AyA + Ay'A + X^-$$

and/or

$$Ay^+X^- + HOS \xrightarrow{k_S} AyOSH^+ + Ay'OSH^+$$

$$AyOSH^+ \xrightarrow{\text{fast}} AyOS$$

$$Ay'OSH^+ \xrightarrow{\text{fast}} Ay'OS$$

of Sneen and Larsen (5-7) extended to a general allylic system. The intermediate shown in Scheme 6 is an intimate allylic ion-pair. The carbonium-ion part of the pair would be a resonance hybrid, an allyl plus species with appropriate alkyl substituents on the three carbons. The positive charge should be very nearly equally distributed over the α- and γ-carbons (11). Note that this mechanism predicts both normal and rearranged products.

Whether a reaction following Scheme 3 or 6 is classified as uni- or bimolecular depends on which stage is rate-controlling. The important features of a bimolecular ion-pair mechanism for allylic compounds are that nonlinear dependency of k_{OBS}/k_{NA} on initial nucleophile concentration should be accompanied by nearly identical distributions for both solvolysis and nucleophile products. The ratio of RA products to ROS products should also be proportional to initial A^- concentration.

In the limiting extreme, a mechanism like that shown in Scheme 6 but for which $k_A A > k_S >> k_R > k_F$, the rate-determining step will be unimolecular, and

the mechanism will be a classical SN1 allylic mechanism. The ratios Ay'OS/AyOS and Ay'A/AyA should still be nearly identical. Kinetic dependency on $[A^-]$ should not be observed, but AyA/AyOS product ratio could still be proportional to initial A^-, when it is present in sufficient excess.

Concurrent, Competitive Mechanisms

It is also possible that solvolysis of AyX could proceed by an ion-pair intermediate like that of Scheme 6 while nucleophilic anions, A^-, could attack AyX directly by an SN2 mechanism. Scheme 7 shows this possibility.

Scheme 7

$$AyX \underset{k_R}{\overset{k_F}{\rightleftharpoons}} Ay^+X^-$$

$$Ay^+X^- \xrightarrow{k_S} \begin{matrix} AyOSH^+ \\ + \\ Ay'OSH^+ \end{matrix} + X^-$$

$$AyOSH^+ \xrightarrow{\text{fast}} AyOS + H^+$$

$$Ay'OSH^+ \xrightarrow{\text{fast}} Ay'OS + H^+$$

$$AyX + A^- \xrightarrow{k_A} AyA + X^-$$

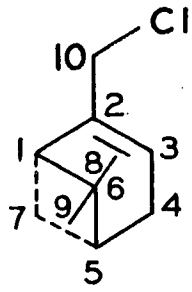
The experimental (pseudo-first-order) rate constant should be a linear function of initial nucleophile concentration. Normal AyA product would not be accompanied by any rearranged Ay'A. Net configuration at the α-carbon of the AyA product would be inverted. (Only if the α-carbon were asymmetric would net inversion or racemization be detectable.) Whether the rate-determining step of

the reaction with solvent is the unimolecular one or the bimolecular one is not directly verifiable by experiment. The important feature of this scheme is that two distinct mechanisms, direct substitution (SN2) and substitution through an ion-pair intermediate operate concurrently and competitively.

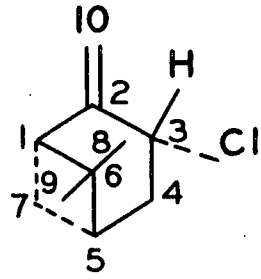
SCOPE OF THIS THESIS

Myrtenyl and trans-pinocarvyl chlorides are allylic chlorides derived from α- and β-pinene, respectively. These four compounds and the two probable products of methanolysis of myrtenyl chloride are shown in Fig. 2. The initial objective of this thesis was a determination of the mechanism of methanolysis of myrtenyl, trans-pinocarvyl and cis-pinocarvyl chlorides. These derivatives were chosen because the sulfonate esters with which Gruenewald worked were so unstable that only cis-pinocarvyl brosylate could be studied (12). Solvolysis reactions of allylic chlorides in mixed aqueous solvents and in ethanol have been studied extensively (9). Methanol has been used less as a reaction medium and reactive solvent than ethanol has. Study of these chlorides in methanol would contribute to the available information about reactions in this solvent.

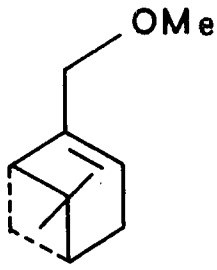
After this thesis was begun, the articles by Sneen and his coworkers (5-7) were published. These authors suggested that ion-pair intermediates may be involved in all nucleophilic substitutions at saturated carbon, not just the SN1-SN2 borderline cases which they have studied. To be generally applicable to all nucleophilic substitutions at saturated carbon atoms, the ion-pair mechanism would have to fit the results from good SN2 systems as well as the borderline cases to which it has been applied. The second objective of this thesis was to further test the scope of this ion-pair mechanism. Myrtenyl chloride is a primary allylic chloride, so it is a typically good SN2 substrate.



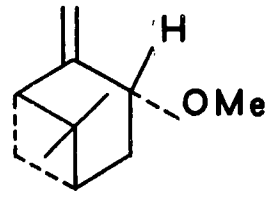
a. Myrtenyl chloride



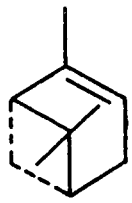
d. <u>trans</u>-Pinocarvyl chloride



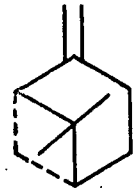
b. Myrtenyl methyl ether



e. <u>trans</u>-Pinocarvyl methyl ether



c. α-Pinene



f. β-Pinene

Figure 2. Compounds of Interest to This Thesis

Nucleophilic substitution can be accompanied by or even outweighed by elimination of HX from RX to form a carbon-carbon double bond (1,3,4). Allylic compounds, however, are less prone to this reaction than are saturated compounds (9). It was thought to be interesting to find out whether myrtenyl chloride can give verbenene (13) or some other diene under the reaction conditions to be employed.

RESULTS AND DISCUSSION

PRODUCTS

Methanolysis rate constants, k_{OBS}, and product distributions are given in Table I. Yield data, given in Appendix B, Table XV, indicate that substitution was quantitative under all conditions studied.

TABLE I

METHANOLYSIS RATE CONSTANTS AND PRODUCT DISTRIBUTION FOR MYRTENYL CHLORIDE AT 35.0°C.[a]

Salt or Nucleophile	$(k_{OBS} \pm \sigma) \times 10^6$, $sec.^{-1}$[b]	Myrtenyl Methyl Ether[c], %
None[d]	3.03 ± 0.03[d]	86 (89[e])
0.05M $LiClO_4$[d]	3.17 ± 0.03	87
0.02M NaOMe + 0.03M $LiClO_4$	4.67 ± 0.08	88
0.035M NaOMe + 0.015M $LiClO_4$	5.48 ± 0.12	91
0.05M NaOMe	7.09 ± 0.13	93
0.3M KOAc	5.17 ± 0.04	66[e,f]

[a] Initial myrtenyl chloride concentrations were all between 0.01 and 0.03M.

[b] These rate constants are for myrtenyl chloride alone. (See p. 47.)

[c] These are averaged experimental results for duplicate runs which contained both myrtenyl and trans-pinocarvyl chloride. (See p. 15.)

[d] These reactions were buffered with 0.02M 2,6-dimethylpyridine.

[e] The myrtenyl chloride used for these runs had only 4% trans-pinocarvyl chloride. The others had 20%. (See p. 15.)

[f] The product mixture also contained 26% myrtenyl acetate. The distribution of ethers was 89% myrtenyl and 11% trans-pinocarvyl methyl ether.

Both normal and rearranged methyl ethers resulted from methanolysis of myrtenyl chloride at 35°C. in methanol buffered with 0.02M 2,6-dimethylpyridine. Conversion (corrected for the isomeric chloride's contribution to the reaction, see p. 15) of myrtenyl chloride to myrtenyl methyl ether was 90% and to trans-pinocarvyl methyl ether was 10%. No cis-pinocarvyl methyl ether was produced. Had it been 1% or more of the products, detection would have been certain at the gas-liquid partition chromatography (GLC) conditions used. Absence of cis-pinocarvyl methyl ether is not surprising. Its absence indicates that the cis- side of C3 is effectively blocked by the C8 methyl group. Gruenewald also found no cis-pinocarvyl products from methanolysis and hydrolysis (in 55% aqueous acetone) of cis-pinocarvyl brosylate (12).

Substitution with rearrangement to the allylic isomer rules out an SN2 mechanism as the sole pathway for methanolysis of myrtenyl chloride. Although a combined SN2-SN2' theory could explain the facts, the possibility of trans-pinocarvyl methyl ether from myrtenyl chloride by an SN2' methanolysis mechanism is extremely unlikely. The observed course of well-documented SN2' reactions is in the other direction (4). That is secondary allylic halides and esters sometimes give primary (rearranged) along with secondary (normal) substitution product. In fact, in well-documented cases (4,9) the SN2' mechanism is concluded to have been responsible for the rearranged product primarily because the kinetic evidence indicated that the reaction was bimolecular. The author is not aware of any solvolysis reaction in the absence of added nucleophiles which was concluded to have proceeded by concurrent SN2 and SN2' mechanisms.

Catchpole and Hughes (15) found 82% γ-methylallyl ethyl ether (rearranged product) from ethanolysis of α-methylallyl chloride. They also found that the

kinetically proved bimolecular reaction between ethoxide and α-methylallyl chloride in ethanol gave 100% α-methylallyl ethyl ether (normal product). Catchpole and Hughes concluded that α-methylallyl chloride was ethanolyzed by an SN1-allylic mechanism and that the SN2 pathway played no role whatsoever. α-Methylallyl chloride is a more promising substrate for an SN2' solvolysis than is myrtenyl chloride. Therefore, it is highly unlikely that concurrent, competitive SN2 and SN2' mechanisms operate for methanolysis of myrtenyl chloride. An SN1 type mechanism seems quite likely for methanolysis of myrtenyl chloride, but a combination of SN1 and SN2 mechanisms cannot be ruled out. That the intermediate is probably not a free allylic carbonium ion, but rather that it is an allylic ion-pair will be demonstrated.

DISTRIBUTION

Calculation

Since myrtenyl chloride could not be completely freed of trans-pinocarvyl chloride, the true product distribution for each chloride had to be calculated. 2,6-Dimethylpyridine-buffered methanolyses of myrtenyl chloride containing 4 and 20% trans-pinocarvyl chloride gave 89 (± 0.5) and 86 (± 0.5)% myrtenyl methyl ether, respectively. The fraction of myrtenyl chloride giving myrtenyl methyl ether, f_{mm}, and the fraction giving trans-pinocarvyl methyl ether, f_{mp}, must add up to 1.00, since only the two ethers were produced. The same will be true for f_{pm}, the fraction of trans-pinocarvyl chloride giving myrtenyl methyl ether and for f_{pp}, the fraction of trans-pinocarvyl chloride giving trans-pinocarvyl methyl ether. When the chloride percentages of a batch are multiplied by the appropriate fractions, and when these products are summed, the result is the percentage of the appropriate ether. Product distribution data from two batches, with different percentages of trans-pinocarvyl chloride, give four

equations in the four unknown fractions. Solution of these four equations gives $f_{\underline{mm}} = 0.90$, $f_{\underline{mp}} = 0.10$, $f_{\underline{pm}} = 0.68$, and $f_{\underline{pp}} = 0.32$. Thus, myrtenyl chloride gives 90% myrtenyl and 10% trans-pinocarvyl methyl ether.

$$96\% \times f_{mm} + 4\% \times f_{pm} = 89\% \text{ myrtenyl methyl ether} \quad (4)$$

$$80\% \times f_{mm} + 20\% \times f_{pm} = 86\% \text{ myrtenyl methyl ether} \quad (5)$$

$$96\% \times f_{mp} + 4\% \times f_{pp} = 11\% \text{ trans-pinocarvyl methyl ether} \quad (6)$$

$$80\% \times f_{mp} + 20\% \times f_{pp} = 14\% \text{ trans-pinocarvyl methyl ether} \quad (7)$$

trans-Pinocarvyl chloride gives 68% myrtenyl and 32% trans-pinocarvyl methyl ether. If the same calculations are performed on myrtenyl methyl ether percentages of 89 and 87, that is, with an error of 1% in the lower percentage, the result is $f_{\underline{mm}} = 0.90$, $f_{\underline{mp}} = 0.10$, $f_{\underline{pm}} = 0.77$, and $f_{\underline{pp}} = 0.23$. The confidence limits on the distribution of myrtenyl chloride's products are quite narrow, but the limits for trans-pinocarvyl chloride are quite wide. This result is reasonable considering the small amount of trans-pinocarvyl chloride present in the reactions.

Significance of Product Spread

A product spread* of this size is not unusual for alcoholysis of allylic chlorides. De Wolfe and Young (9) and de la Mare (16) have reviewed the problem of product spread. They have suggested two possible explanations. Both are reasoned inductively from the fact that product spread decreases as the polarity (and presumably the ability to promote ionization and ion-pair separation) of the solvent increases. The theories are that product spread is due to incursion of

*Product spread was defined by De Wolfe and Young (9) as the proportion of primary solvolysis product from primary allylic reactant less the proportion of primary solvolysis product from secondary reactant. The difference for myrtenyl and trans-pinocarvyl chlorides is 90-68 = 22%.

an SN2 mechanism in less polar solvents, or that the ion-pair of one allylomer is less stable and reacts before reaching the lowest available energy state in less polar solvents. Either mechanism fits all the data covered by these reviewers (9,16). The most logical reason to choose one over the other is that an SN2 incursion should not be energetically favorable under conditions which really favor C-X bond heterolysis (the SN1 mechanism). The commonly used solvolysis solvents are quite polar. For this reason the author prefers the intermediacy of a less stable, ion-pair for myrtenyl chloride than for trans-pinocarvyl chloride in methanol. The presence of product spread for a pair of allylomers is not considered contradictory to an SN1 solvolysis mechanism (9).

Production of trans- but not of cis-pinocarvyl methyl ether from trans-pinocarvyl chloride indicates that trans-pinocarvyl chloride's methanolysis intermediate must be a relatively free allylic carbonium-ion or a solvent separated ion-pair. The chloride ion must be out of the way of attack by methanol from the side where chloride was originally attached. Production of such a small percentage of trans-pinocarvyl methyl ether from myrtenyl chloride suggests that myrtenyl chloride's methanolysis intermediate is not a free allylic carbonium-ion. Methanol must attack before the chloride ion leaves the solvent cage (17) most of the time. Methanol's approach to C3 to form trans-pinocarvyl methyl ether is hindered more for myrtenyl chloride than for trans-pinocarvyl chloride. Thus, myrtenyl chloride's methanolysis intermediate must be an intimate ion-pair and not a free allylic carbonium-ion.

RATE CONSTANTS

The methanolysis rate constants indicate that the rate-determining step for methanolysis is more energetic for myrtenyl chloride than it is for trans-pinocarvyl chloride, which reacts five times as fast as myrtenyl chloride under

identical methanolysis conditions. Rate constants are 3.03×10^{-6} sec.$^{-1}$ for myrtenyl and 15.4×10^{-6} sec.$^{-1}$ for trans-pinocarvyl chloride. This evidence also indicates that myrtenyl chloride's methanolysis intermediate is less free and therefore probably an intimate ion-pair rather than a free allylic carbonium-ion.

SALT EFFECT

In the following sections the effects of sodium methoxide and potassium acetate upon both k_{OBS} and the product ratio will be discussed. To accurately evaluate the cause of changes in k_{OBS} or the product distribution in the presence of methoxide or acetate requires knowledge of the salt effect of a nonnucleophilic species for comparison. Duplicate kinetic runs were made with 0.05M lithium perchlorate in methanol buffered with 0.02M 2,6-dimethylpyridine at 35.0°C. Lithium perchlorate caused no significant change in product distribution for myrtenyl chloride (Table I). The slight increase of k_{OBS}, to $(3.17 \pm 0.03) \times 10^{-6}$ sec.$^{-1}$, gives a b value of 0.92M^{-1} in the Winstein salt effect equation (18)

$$k_{OBS} = k_m(1 + b[salt]) \qquad (8)$$

where k_{OBS} is the observed solvolysis rate constant with salt present, k_m is k_{OBS} with no salt present, b is the salt effect coefficient, and [salt] is the stoichiometric salt concentration. Individual b values have little significance by themselves. They do, however, tend to be of the order of magnitude of 1M^{-1} for SN1 solvolyses. Methanolysis of cis-pinocarvyl brosylate (12), and 25- and 30% aqueous dioxane hydrolysis of 2-octyl mesylate (5) gave b values of 2.09, 1.15, and 1.04M^{-1}, respectively. While it proves nothing at this point, a b value of 0.92M^{-1} is consistent with an SN1 mechanism. The significance of b

for lithium perchlorate will become apparent when the results of methoxide and acetate experiments are discussed.

SODIUM METHOXIDE

Sodium methoxide caused a percentage increase of myrtenyl methyl ether (Table I). The plot in Fig. 3 of k_{OBS} at 35.0°C. *vs.* initial sodium methoxide concentration at constant ionic strength gave a straight line,

$$k_{OBS} = k_s + k_{OMe}[OMe^-]. \qquad (9)$$

The slope, $(75.9 \pm 6.9) \times 10^{-6}$ M^{-1} $sec.^{-1}$, is the second-order (SN2) rate constant, k_{OMe}, at 35.0°C., for attack of methoxide ion on myrtenyl chloride (or its solvolysis intermediate). The intercept is k_s, the methanolysis rate constant in the presence of 0.05M salt. The value calculated was 3.13×10^{-6} $sec.^{-1}$. This agrees very well with the experimental value 3.17×10^{-6} $sec.^{-1}$ in Table I. Calculations of k_{OMe}, its standard deviation, and of k_s were done by least squares regression (19) of k_{OBS} on initial sodium methoxide concentration. To get good pseudo-first-order kinetics, initial sodium methoxide concentration was always at least twice the initial myrtenyl chloride concentration. Ionic strength was maintained at the same level throughout the series of runs by adding enough lithium perchlorate to bring the total salt concentration to 0.05M. This was done so that the usually observed decrease in SN2 rate constant with increasing nucleophile (or total salt) concentration (20,21) would be eliminated. It is important to eliminate salt effects due to changes in initial methoxide concentration throughout the series of runs so that changes which are found can be clearly attributed to the change in initial methoxide concentration. This also makes it unnecessary to divide Equation (9) by k_s.

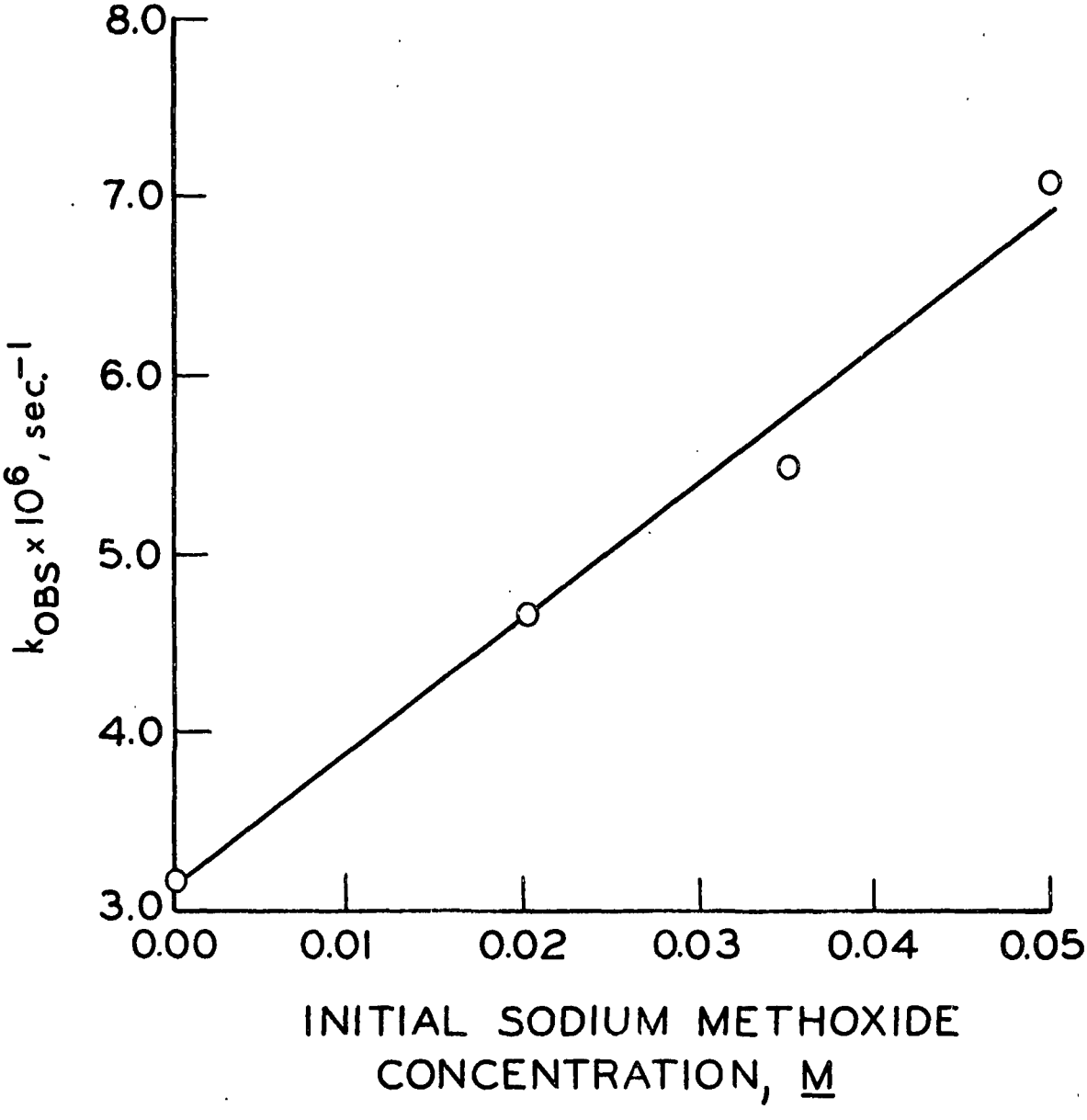


Figure 3. Plot of k_{OBS} at 35.0°C. vs. Initial Sodium Methoxide Concentration

The results of methanolysis with methoxide ion present do not fit the SN1 hypothesis, which requires reaction with lyate ion to be zero-order not first-order, with respect to lyate ion. The possibility that the ion-pair methanolysis intermediate, rather than myrtenyl chloride is attacked by methoxide cannot be ruled out yet. This theory can, however, be eliminated on consideration of further evidence.

Table I shows that increased amounts of myrtenyl methyl ether resulted when initial sodium methoxide concentration was increased. This increase can be assigned to reaction of myrtenyl chloride with sodium methoxide. Since these runs also contained some trans-pinocarvyl chloride, it is necessary to explore the possibility that some of the percentage increase of myrtenyl methyl ether could be due to SN2' reaction of methoxide with trans-pinocarvyl chloride. That this is not the case is suggested by Catchpole and Hughes' work (15) on α-methyl allyl chloride with ethoxide in ethanol. α-Methyl allyl chloride should be a favorable SN2' substrate. It gave only α-methyl allyl ethyl ether (see p. 15). The allylic portion of trans-pinocarvyl chloride is not significantly different structurally from other secondary allylic compounds. Thus, an SN2' reaction with an alkoxide should not be accelerated relative to other secondary allylic compounds. Its rate would be insignificant compared to the rate of methanolysis of trans-pinocarvyl chloride, $(15.4 \pm 0.8) \times 10^{-6}$ sec.$^{-1}$ SN2 reaction of methoxide with trans-pinocarvyl chloride should be strongly hindered by the bridge methyl group. No cis-pinocarvyl methyl ether (within experimental error of 1%) was produced, not even in the presence of 0.05M sodium methoxide. It is reasonable to expect trans-pinocarvyl chloride to react with methoxide only through its methanolysis intermediate (not by SN2 or SN2' mechanisms) and to give the same product distribution with methoxide as it gives

with methanol of equal ionic strength. Thus, the product distribution from trans-pinocarvyl chloride should not be changed by methoxide.

At constant ionic strength the distribution of methanolysis products should remain unchanged as initial methoxide concentration is varied. The methanolysis product conversion factors (see p. 16) should remain 0.90, 0.10, 0.68, and 0.32. Further, if methoxide attacks only myrtenyl chloride (Scheme 7), but not its methanolysis intermediate, the percentage increase of myrtenyl methyl ether evident in Table I should be related to the increase of initial sodium methoxide. Conversely, exclusive attack of methoxide on the methanolysis intermediate (Scheme 6) should cause a rate increase without appreciably changing the product distribution. Should these two mechanisms compete effectively, the percentage increase of myrtenyl methyl ether should be significantly less than what the rate constants predict. Table II gives the percentage of myrtenyl methyl ether predicted from

$$M = yf_{mm}MyCl_o + zMyCl_o + f_{pm}PiCl_o \qquad (10)$$

where M is total percentage myrtenyl methyl ether, y is the fraction of myrtenyl chloride reacting with methanol, f_{mm} is the fraction of myrtenyl chloride converted to myrtenyl methyl ether by methanolysis, $MyCl_o$ is the initial percentage myrtenyl chloride, z is the fraction of myrtenyl chloride reacting with sodium methoxide, f_{pm} is the fraction of trans-pinocarvyl chloride converted to myrtenyl methyl ether by methanolysis, and $PiCl_o$ is the initial percentage trans-pinocarvyl chloride. Since y is the fraction methanolyzed,

$$y = k_s/k_{OBS} \qquad (11)$$

TABLE II

COMPARISON OF EXPERIMENTAL AND CALCULATED PERCENTAGES OF MYRTENYL METHYL ETHER AS A FUNCTION OF INITIAL METHOXIDE CONCENTRATION

MeO^{-2}, M	% MyOMe[b], calculated	% MyOMe[c], experimental
0.000	86	87
0.020	89	88
0.035	90	91
0.050	91	93

[a] Initial sodium methoxide concentration. Initial myrtenyl chloride concentration was between 0.01 and 0.03M for all runs.

[b] Myrtenyl methyl ether, percentage of total products. Calculated from Equation (15).

[c] Myrtenyl methyl ether, percentage of total products. Experimental values reported in Table I.

and since z is the fraction reacting with methoxide,

$$z = k_{OMe}[OMe^-] / k_{OBS}. \tag{12}$$

From Equation (9),

$$k_{OMe}[OMe^-] = k_{OBS} - k_s, \tag{13}$$

and

$$z = \frac{k_{OBS} - k_s}{k_{OBS}}. \tag{14}$$

The myrtenyl chloride used for these runs was actually 80% myrtenyl chloride and 20% trans-pinocarvyl chloride (see p. 15). Substituting these data, the conversion fractions, and Equations (11) and (14) in Equation (10) gives

$$M = \frac{k_s}{k_{OBS}} 72\% + \frac{k_{OBS}-k_s}{k_{OBS}} 80\% + 14\%. \qquad (15)$$

M values calculated from Equation (15) are compared with the experimental results in Table II.

If the least squares rate constants, $k_{OMe} = 75.9 \times 10^{-6} M^{-1}$ sec.$^{-1}$ and $k_s = 3.1 \times 10^{-6}$ sec.$^{-1}$ are used along with the known initial concentrations of sodium methoxide to calculate the product distribution, the calculated percentages of myrtenyl methyl ether are the same as the values calculated from the experimental rate constants, k_{OBS}.

The excellent agreement between the calculated and experimental myrtenyl methyl ether percentages rules out any significant contribution to the reaction pathway by Scheme 6. Finding as much myrtenyl methyl ether experimentally as the rate increase predicts means that the rate increase due to methoxide is accompanied by a one for one increase in percentage myrtenyl methyl ether. Direct attack of methoxide on myrtenyl chloride (Scheme 7) but not on the methanolysis intermediate (Scheme 6) is the best explanation. This is so because attack on the intermediate by methoxide should give about the same distribution of methyl ethers as attack by solvent.

Figure 3 shows that k_{OBS} is a linear function of initial methoxide at constant ionic strength. The kinetics of Scheme 6 with $A^- = OMe^-$ are essentially the same as those of Sneen and Robbins (7) for α-phenethyl chloride in ethanolic ethoxide. Sneen and Larsen's ion-pair theory (5,7) predicts that k_{OBS} should not be linear with initial methoxide but should be concave downward. The experimental result of this work is that k_{OBS} vs. initial methoxide at constant

ionic strength is a straight line. Methanolysis of myrtenyl chloride in the presence of sodium methoxide fits Scheme 7 (SN1 type solvolysis concurrent with SN2 attack by methoxide). This reaction does not fit Scheme 6 (competitive attack by both methanol and methoxide on the ion-pair intermediate).

POTASSIUM ACETATE

In the presence of 0.3M potassium acetate, myrtenyl chloride gave the same ratio of methanolysis products as with no salt or with lithium perchlorate (Table I). The rate constant, k_{OBS}, however, increased to (5.17 ± 0.04) x 10^{-6} sec.$^{-1}$ (Table I), and 26% of the product was myrtenyl acetate. Assuming that the salt effect of potassium acetate on k_m is about the same as that of lithium perchlorate, the second-order rate constant, k_{OAc}, for reaction of acetate with myrtenyl chloride (but not with the ion-pair methanolysis intermediate) can be calculated from

$$k_{OBS} = k_m(1 + 0.92[OAc^-]) + k_{OAc}[OA_c^-], \qquad (16)$$

where k_m is k_{OBS} with no salt present.

From this equation k_{OAc} is 4.3 x $10^{-6}M^{-1}$ sec.$^{-1}$. Calculation of k_{OAc} from this equation assumes that Scheme 7 is followed, not Scheme 6. If this hypothesis is correct, the percentage of myrtenyl acetate in the product should be predicted by the ratio of $k_{OAc}[OAc^-]$ / k_{OBS}. The rate constants predict 25% myrtenyl acetate and 26% was found. Scheme 6 competing significantly with Scheme 7 would cause the experimental amount to be less than the predicted amount. Operation of Scheme 6 (to any significant degree) would probably also cause some trans-pinocarvyl acetate to be produced. No trans-pinocarvyl acetate was found. By

analogy with the distribution of methanolysis products, the expected quantity is 10% of the acetate product or about 3% of the total if myrtenyl chloride had reacted with acetate entirely by Scheme 6. Had trans- (or cis-) pinocarvyl acetate been $\geq$ 1% of the total, they surely would have been detected by the GLC conditions used.

Attack by both solvent and nucleophiles on the same intermediate is ruled out, as well as SN1 alone or SN2-SN2' combined mechanisms. A combination of methanolysis through an allylic ion-pair intermediate (probably an intimate ion-pair) by an SN1 mechanism accompanied by SN2 type attack of either acetate or methoxide ions on myrtenyl chloride, not on the methanolysis-intermediate, fits all the facts.

It appears that the ion-pair intermediate in SN2 reactions is restricted somewhat from the generality envisioned by Sneen and his coworkers (5,6,7). They have concluded that the apparent competition between SN1 and SN2 mechanisms found for 2-octyl mesylate (5), p-methoxy-benzyl chloride (6), benzoyl chloride (6), and α-phenethyl chloride (7) can be explained by attack of both solvent and added nucleophiles on a configurationally stable ion-pair intermediate. They have not yet reported on an allylic compound. Nor have they reported on so-called good SN2 substrates such as methyl or primary alkyl halides.

PRODUCT STABILITY

Suitable control reactions showed that myrtenyl and trans-pinocarvyl methyl ethers and acetates are stable to the reaction conditions employed. Myrtenyl acetate slowly deacetylated to give myrtenol. The pseudo-first-order rate constant for disappearance of myrtenyl acetate was 1.1×10^{-7} sec.$^{-1}$ at 35.0°C. This is 2×10^{-4} times k_m for myrtenyl chloride in the presence of 0.3M potassium acetate.

Myrtenyl methyl ether was not stable to methanolic hydrogen chloride. At least seven new GLC peaks were found after ten days exposure of myrtenyl methyl ether (initially 0.1M) to 0.1M methanolic hydrogen chloride at 35°C. Only a very small fraction of the initial concentration of myrtenyl methyl ether remained. For this reason it was necessary to buffer the methanolyses which had neither sodium methoxide nor potassium acetate present.

The buffer chosen was 2,6-dimethylpyridine. This hindered amine was found to be unreactive toward myrtenyl chloride in deuterochloroform solution. Nuclear magnetic resonance (NMR) spectra run before and after seven days at 35°C. were the same. Further evidence of no reaction between the chloride and the amine is the fact that quantitative yields of methyl ether substitution products were obtained, and that the methyl ether product distribution was not significantly different with 2,6-dimethylpyridine than with potassium acetate. It was concluded that no reaction occurred between myrtenyl chloride and 2,6-dimethylpyridine.

FURTHER STUDIES IN DISPLACEMENT REACTIONS OF PINENE DERIVATIVES

trans-Pinocarvyl chloride might react with nucleophiles such as methoxide and acetate through an ion-pair intermediate, according to Scheme 6. Hydrolysis of myrtenyl chloride in aqueous dioxane in the presence of a strong nucleophile might also provide a system capable of reacting by an ion-pair mechanism.

CONCLUSIONS

In the presence of nucleophilic anions in methanol, myrtenyl chloride reacts by two mechanisms. Reaction with solvent methanol *via* an allylic ion-pair intermediate proceeds by an SN1 mechanism. The intermediate is an allylic ion-pair rather than a free allylic carbonium-ion. Reactions with potassium acetate and sodium methoxide proceed by an SN2 mechanism. Modification of Sneen and Larsen's hypothesis, that all reactions of nucleophilic substitution at a saturated carbon atom proceed *via* an ion-pair mechanism (5,7), is now necessary.

EXPERIMENTAL PROCEDURES

MATERIALS

METHANOL

Reagent-grade methanol was dried by reaction with magnesium turnings (5 g./l. of methanol) followed by distillation. It was protected from atmospheric moisture by a potassium hydroxide drying tube on the inlet to the siphon bottle. This method is essentially that of Lund and Bjerrum, as reported by Perrin, et al. (22). Water concentration was tested by GLC on a 6 ft. by 1/4 in. Porapak-Q column. Temperature was 155°C. Flow was 60 ml.min.$^{-1}$. Filament current was 150 ma. The instrument was a Varian Aerograph 202C with thermal conductivity detector. Standards were prepared by dilution of 0.1 and 0.01 ml. aliquots of freshly boiled and cooled, distilled water to 10 ml. in volumetric flasks with dried, distilled methanol. These, and methanol to which no water was added, were put in 15-ml. vials* and stoppered with serum caps. Aliquots of 10 to 25 µl. were withdrawn through the serum cap and injected into the gas chromatograph.

The peak height response factor (phrf) was calculated from the slope of the relative-peak-height vs. percent-water-added plot in Fig. 4. The result was phrf = 11.2. Thus, for an unknown, the relative water peak height (methanol peak was used as internal standard) was multiplied by 11.2 to get the percentage (by volume) water present. The methanol used for kinetic and product studies had less than 0.2% water, unless otherwise stated.

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*The vials were prepared as for kinetic runs by the technique described in the methods section.

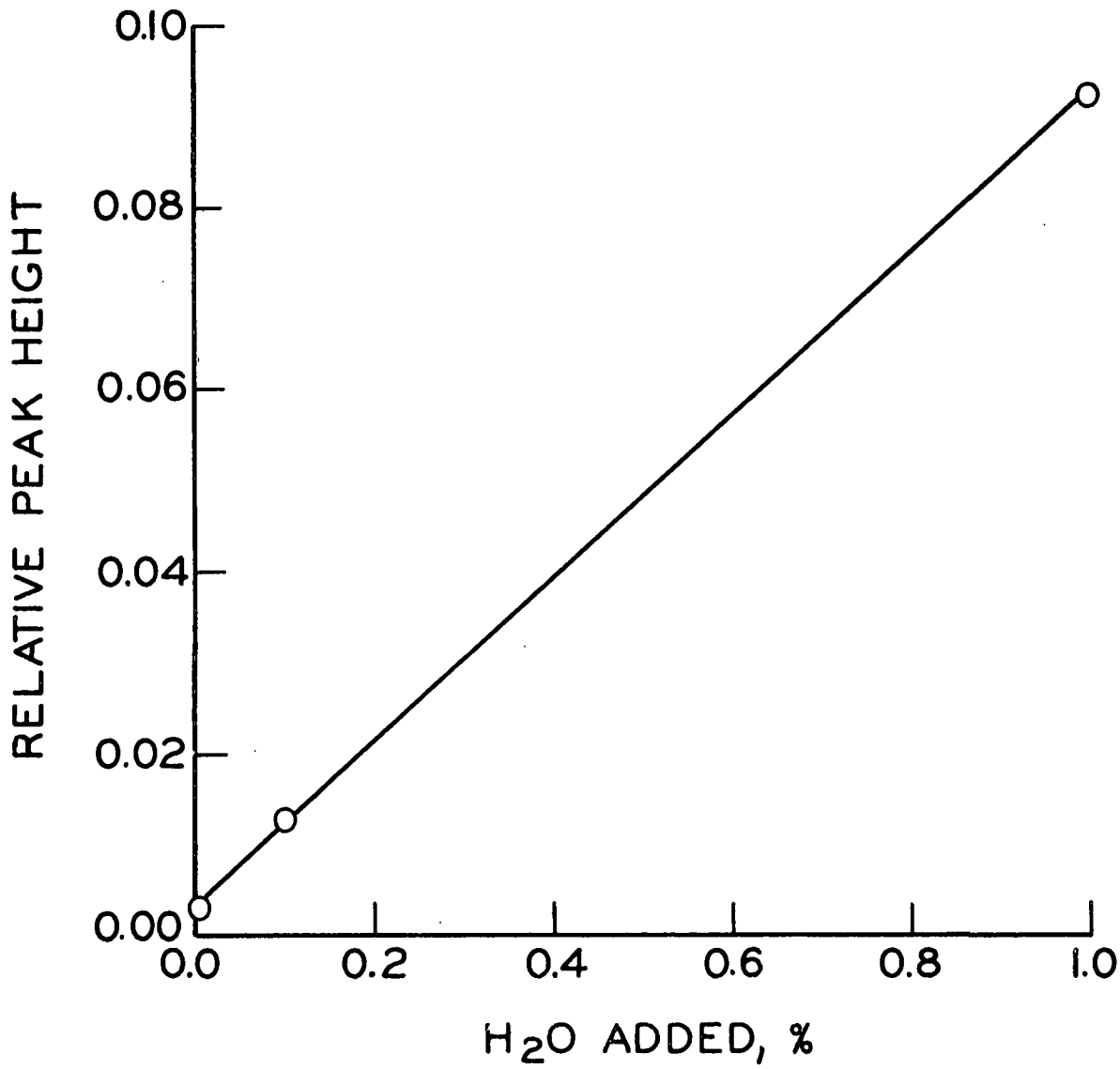

Figure 4. Standard Curve for GLC Analysis of H_2O in MeOH. Response Factor = 11.2 = 1/Slope

SODIUM METHOXIDE

A 0.5M solution of methanolic sodium methoxide was prepared and kept for stock. Sodium metal (approximately 5 g.) was cut in small cubes and scraped free of white powdery coating, then placed in fresh kerosene. Each piece was thoroughly rinsed in dry methanol until all surfaces were bright again, then dropped through a short water-cooled condenser into 250 ml. dry methanol in a 500-ml. round-bottom flask. A drierite drying tube attached to a standard taper joint was kept in the top of the condenser during this preparation. Removal for only a few seconds was required for addition of each piece of sodium. Following the reaction, aliquots were titrated and sufficient dry methanol was added to bring the concentration to 0.5M. The solution was stored in a screw top bottle and dispensed by pipet.

OTHER SALTS

Methanolic solutions of lithium perchlorate, lithium chloride, potassium acetate, and sodium chloride were prepared by dissolving carefully weighed, oven-dried salts in dry methanol. The only salt which required special handling was lithium perchlorate. It was weighed and put in the volumetric flask in a dry box, then diluted with dry methanol outside the dry box.

2,6-DIMETHYLPYRIDINE

Eastman Yellow Label 2,6-dimethylpyridine was distilled through a 40-cm. Vigreux column. Following a forerun, material with a boiling range (uncorrected) of 143 to 144°C. was retained. The reported boiling point is 143°C. (23). The author thanks David P. Hultman for his generous gift of this distilled material.

4-METHOXYTOLUENE

This material was obtained from K and K Labs and was found to be pure by GLC. This generous gift from James Farrand was used without further purification.

CHLOROFORM

The method of Reynolds and Evans (24) was modified slightly to produce dry alcohol-free chloroform for lead tetraacetate oxidation of β-pinene. One 5-pt. jug of reagent-grade (or recovered, used) chloroform was stirred mechanically for at least one hour with 1 l. each of the following: 18% sulfuric acid, water, saturated sodium bicarbonate, and water. The washed chloroform was shaken with anhydrous calcium chloride, filtered and dried overnight with Drierite. It was filtered, dry nitrogen was bubbled through it and permitted to fill the still and collector. Distillation through a 3-ft. glass column filled with 6-mm. glass Raschig rings gave material boiling from 59.5 to 60.5°C. (uncorrected); literature boiling point 61.2°C. (23). The still was all glass and was protected from atmospheric moisture by a Drierite-filled drying tube. The forerun and pot residue, about 1 l., were combined with fresh chloroform and repurified. Yield of purified chloroform was 1 l., 42% of the starting amount. The distillate was stored in ground-glass-stoppered 1-l. bottles sealed with Parafilm. This prevented phosgene formation and gave material in which lead tetraacetate did not decompose appreciably.

MYRTENYL AND trans-PINOCARVYL ACETATES

The title compounds were synthesized in 50% yield from β-pinene and lead tetraacetate by a modification of the procedure given by Gruenewald and Johnson (25). Since the reaction had to be run several times to accumulate sufficient material, some attempt at maximization of yield was made. Specifically,

temperature of the reaction solution was maintained below -10°C. during addition of lead tetraacetate and for at least two hours afterwards to obtain 40-50% yields (based on unrecovered β-pinene). Also, complete solution of lead tetraacetate in chloroform required addition of enough acetic acid to just cover the solid lead tetraacetate. Typically, 250 g. (0.56 mole) lead tetraacetate (Matheson, Coleman and Bell, reagent) was just covered with glacial acetic acid and dissolved in 800 ml. purified chloroform with heating. This solution, kept warm by a heating tape around the dropping funnel, was added during two hours to the stirred solution of 80 g. (0.59 mole) β-pinene (Aldrich, 95% by GLC) in 300 ml. purified chloroform in a 3-neck, 2-l., round-bottom flask. The reaction solution was cooled by an ice-methanol bath to maintain reaction temperature between -10 and -15°C. Stirring continued for two hours at -10 to -20°C. The reaction solution was always clear and only faintly yellow at this point when good yields (40-50% of theory) were obtained. When the reaction temperature was permitted to rise above 0°C., precipitation of lead diacetate began before all the lead tetraacetate was added, and yields of monoacetate fraction were typically 20-30% of theory.

Following the two-hour stirring period at low temperature, the reaction solution was stirred while it warmed up to room temperature, usually overnight. Lead diacetate was filtered from the chloroform-acetic acid solution, and the filtrate was concentrated to about 500 ml. It was then washed with water until a drop of concentrated sulfuric acid in the wash water caused no white precipitate to appear. The chloroform solution was then washed once with an equal volume of 5% aqueous sodium bicarbonate solution. This aqueous phase always remained alkaline to litmus. The acetates were recovered from the washed and dried chloroform solution by concentration at reduced pressure. Fractional distillation of crude acetates at reduced pressure gave a monoacetate fraction

boiling from 46 to 70°C. at 0.2 mm. The best yield recorded was 47 g. (0.24 mole). Unreacted β-pinene (20 g., 0.15 mole) was recovered. This yield, based on unrecovered hydrocarbon, is 59% of theory. GLC of this monoacetate fraction on Carbowax 20M indicated a distribution of 20% myrtenyl and 80% trans-pinocarvyl acetate. Temperature was 125°C. Flow was 30 ml.min.$^{-1}$ nitrogen. Hydrogen flow to the flame ionization detector (FID) was 30 ml.min.$^{-1}$. The instrument was a Varian Aerograph 1200-1.

Distillation of trans-pinocarvyl acetate to give a pure fraction boiling at 112-113°C. at 12 mm. Hg was possible. Separation of pure myrtenyl acetate proved impossible; so it was synthesized from distilled myrtenol. The pertinent NMR signals for trans-pinocarvyl acetate are given in Table III. Chemical shift assignments given are based on the general principles of NMR spectroscopy given in Silverstein and Bassler (26).

Myrtenol (9.90 g., 0.0651 mole, see below for source) was dissolved in 26 ml. pyridine, and 13 ml. (0.13 mole) acetic anhydride was added. This mixture warmed slightly upon mixing. It was left at room temperature in a stoppered flask for three days. The reaction was poured into 500 ml. ice and water with stirring. After fifteen minutes stirring the cream-colored ice-water emulsion was extracted once with 200 ml. and twice with 150 ml. chloroform. The combined chloroform extracts were washed four times with 100-ml. portions of M hydrochloric acid; until the aqueous phase remained acid. The chloroform layer was then washed with 100 ml. water and 100 ml. saturated aqueous sodium bicarbonate, which remained alkaline. The chloroform solution was dried twice over Drierite and concentrated on a rotary vacuum evaporator. Fractional distillation on an 18-in. spinning-band column at reduced pressure gave three fractions. The third boiled

TABLE III

NMR SPECTRUM OF trans-PINOCARVYL ACETATE[a]

Chemical Shift, α, p.p.m.	Integral Height, mm.	Number of Protons	J,Hz, and multiplicity[b]	Assignment[c]
5.56	7	1	8,D	Methine, α- to OAc
5.03	7	1	1,T	Vinyl, cis- to CHOAc
4.87	8	1	1,T	Vinyl, trans- to CHOAc
2.7-1.5	45	6	M	Other ring H
2.04	22	3	S	Methyl of OAc
1.28	22	3	S	Methyl, trans- to CHOAc
0.70	22	3	S	Methyl, cis- to CHOAc

[a] 60 MHz NMR spectrum run on a Varian A60A NMR spectrometer at normal probe temperature of 45°C. Concentration was 15% (v/v) in $CDCl_3$ with 1% tetramethylsilane internal standard.

[b] S = singlet, D = doublet, T = triplet, M = multiplet.

[c] Reference (26).

at 46°C. at 0.14 mm. Hg. It was 99% myrtenyl acetate as determined by GLC on Carbowax 20M at 150°C. and 30 p.s.i. nitrogen. The pertinent signals of the NMR spectrum are given in Table IV. Zweifel and Whitney (13) give α values of 4.74 and 5.50 p.p.m. for the allylic and vinyl protons, respectively, of myrtenyl acetate in carbon tetrachloride.

TABLE IV

NMR SPECTRUM OF MYRTENYL ACETATE[a]

Chemical Shift, α, p.p.m.	Integral Height, mm.	Number of Protons	J,Hz, and multiplicity[b]	Assignment[c]
5.57	9	1	1.5,M	Vinyl
4.47	18	2	1.5,Q	Methylene, α- to OAc and vinyl
2.6-1.9	48	5	M	Other ring H
2.05	30	3	S	Methyl of OAc
1.30	31	3	S	Methyl, trans- to vinyl
1.20	8	1	8.5,D	One of methylene H's on cyclobutane ring, cis- to vinyl
0.83	27	3	S	Methyl, cis- to vinyl

[a] 60 MHz NMR spectrum run on a Varian A60A NMR spectrometer at normal probe temperature of 45°C. Concentration was 15% (v/v) in $CDCl_3$ with 1% tetramethylsilane internal standard.

[b] S = singlet, Q = quartet, M = multiplet.

[c] Reference (26).

MYRTENOL AND trans-PINOCARVEOL

Typically, two batches of monoacetates were combined and deesterified by sodium methoxide in methanol to give 82% of the theoretical yield of myrtenol and trans-pinocarveol in the same ratio (19:81, by weight of distillate fractions). Combined monoacetate fractions weighing 129 g. (0.665 mole) were dissolved in 1500 ml. 0.07M methanolic sodium methoxide. Methanol and methyl acetate were distilled slowly from the reaction solution for twenty-four hours, until neither distillate nor reaction solution gave a ferric hydroxamate test for esters (27). The

remaining 500-1000 ml. methanolic reaction solution was poured into an equal volume of water and extracted thoroughly with practical heptane. The washed and dried (over anhydrous magnesium sulfate) heptane solution was concentrated, and the resulting alcohols were fractionally distilled to give 68.9 g. of 95% pure trans-pinocarveol, b.p. 31-35°C. at 0.06 mm. GLC on a 10-ft. by 1/8-in. 10%-TCEP column at 130°C. and 40 ml.min.$^{-1}$ nitrogen established the purity. The 60 MHz NMR spectrum had the readily assignable signals listed in Table V.

TABLE V

NMR SPECTRUM OF trans-PINOCARVEOL[a]

Chemical Shift, α, p.p.m.	Integral Height, mm.	Number of Protons	J,Hz, and multiplicity[b]	Assignment[c]
4.98	11	1	S	Vinyl, cis- to OH
4.80	11	1	S	Vinyl, trans- to OH
4.42	11	1	6.75,D	Methine, α- to OH
2.7-1.6	66	6	M	Other ring H
1.73	10	1	S	OH[d]
1.28	35	3	S	Methyl, trans- to OH
0.65	35	3	S	Methyl, cis- to OH

[a] 60 MHz NMR spectrum run on a Varian A60A NMR spectrometer at normal probe temperature of 45°C. Concentration was 15% (v/v) in $CDCl_3$ with 1% tetramethylsilane internal standard.

[b] S = singlet, D = doublet, M = multiplet.

[c] Reference (26).

[d] This signal disappeared completely after shaking the $CDCl_3$ solution with a drop of D_2O for several minutes.

Continued distillation gave a 3.3-g. intermediate fraction boiling from 33 to 42°C. at 0.06 mm. GLC indicated about 2/3 trans-pinocarveol and 1/3 myrtenol.

Finally 16.4 g. myrtenol (98% by GLC) was obtained, b.p. 42-47°C. at 0.06 mm. The 60 MHz NMR spectrum had the readily assignable signals listed in Table VI. Zweifel and Whitney (13) report α values of 5.33 and 3.80 p.p.m. for the C3 and C10 protons, respectively, in carbon tetrachloride.

TABLE VI

NMR SPECTRUM OF MYRTENOL[a]

Chemical Shift, α, p.p.m.	Integral Height, mm.	Number of Protons	J,Hz, and multiplicity[b]	Assignment[c]
5.48	12	1	1.5,M	Vinyl
3.90	24	2	1.5,Q	Methylene, α- to OH and vinyl
2.7-2.0	59	5	M	Other ring H
1.76	12	1	S	OH[d]
1.30	42	3	S	Methyl, trans- to vinyl
1.18	9	1	8.3,D	One of methylene H's of cyclobutane ring, cis- to vinyl
0.85	38	3	S	Methyl, cis- to vinyl

[a] 60 MHz NMR spectrum run on a Varian A60A NMR spectrometer at normal probe temperature of 45°C. Concentration was 15% (v/v) in $CDCl_3$ with 1% tetramethylsilane internal standard.

[b] S = singlet, D = doublet, Q = quartet, M = multiplet.

[c] Reference (26).

[d] This signal disappeared completely after shaking the $CDCl_3$ solution with a drop of D_2O for several minutes.

MYRTENYL CHLORIDE

Myrtenyl chloride was synthesized in 40-60% yields by reaction of trans-pinocarveol with thionyl chloride in ether at 0°C. The procedure employed was

essentially that described by Young, et al. (28) for α- and γ-methylallyl chlorides. Separation of myrtenyl chloride from unreacted trans-pinocarveol was effected by fractional distillation on an 18-in. annular spinning-band column at reduced pressure. It boiled at 52°C. at 2 mm.; literature boiling point 55-57°C. at 2 mm. (29). The NMR spectrum given in Table VII was identical with the NMR spectrum of myrtenyl chloride prepared by chlorination of β-pinene (29). Purity of myrtenyl chloride synthesized from trans-pinocarveol and thionyl chloride was 80 to 96%.

TABLE VII

NMR SPECTRUM OF MYRTENYL CHLORIDE[a]

Chemical Shift, α, p.p.m.	Integral Height, mm.	Number of Protons	J,Hz, and multiplicity[b]	Assignment[c]
5.62	11	1	1.5,M	Vinyl
3.98	24	2	1.5,Q	Methylene, α- to Cl and vinyl
2.7-2.0	61	5	M	Other ring H
1.32	37	3	S	Methyl, trans- to vinyl
1.17	10	1	8.4,D	One methylene H of cyclobutane ring, cis- to vinyl
0.83	36	3	S	Methyl, cis- to vinyl

[a] 60 MHz NMR spectrum run on a Varian A60A NMR spectrometer at normal probe temperature of 45°C. Concentration was 15% (v/v) in $CDCl_3$ with 1% tetramethylsilane internal standard.

[b] S = singlet, D = doublet, Q = quartet, M = multiplet.

[c] Reference (26).

trans-PINOCARVYL CHLORIDE

Synthesis from myrtenol and thionyl chloride was attempted by the same procedure as for myrtenyl chloride. The crude reaction product (about 50% of theory) gave NMR signals with α values and peak shapes similar to those of trans-pinocarveol for the H α- to chlorine, the vinyl H's and the bridge methyl H's. The integral weights are correct for a trans-pinocarvyl rather than myrtenyl derivative. Table VIII gives the pertinent NMR signals. When fractional distillation on an 18-in. annular spinning-band column at 0.2-0.3 mm. Hg was attempted, only 20% of the worked up reaction product was recovered. It gave the same NMR spectrum as myrtenyl chloride. The organic material from the dry-ice and acetone trap was analyzed by GLC and also found to be myrtenyl chloride. It was about 2% of the crude trans-pinocarvyl chloride reaction product.

TABLE VIII

PARTIAL NMR SPECTRUM OF trans-PINOCARVYL CHLORIDE[a]

Chemical Shift, α, p.p.m.	Integral Height, mm.	Number of Protons	J,Hz, and multiplicity[b]	Assignment[c]
5.12	5	1	S	Vinyl, cis- to CHCl
4.91	5	1	S	Vinyl, trans- to CHCl
4.79	5	1	8,D	Methine, α- to Cl and vinyl
1.28	32[d]	3	S	Methyl, trans- to Cl
0.65	15	3	S	Methyl, cis- to Cl

[a] 60 MHz NMR spectrum run on a Varian A60A NMR spectrometer at normal probe temperature of 45°C. Concentration was 15% (v/v) in $CDCl_3$ with 1% tetramethylsilane internal standard.

[b] S = singlet, D = doublet.

[c] Reference (26).

[d] The double weight of this signal is due to myrtenyl chloride and/or unreacted myrtenol present in this crude reaction product (approximately 50% trans-pinocarbyl chloride).

MYRTENYL METHYL ETHER

Myrtenyl chloride (3.4 g., 20 millimoles) was dissolved in 25 ml. M methanolic sodium methoxide and the solution was refluxed overnight. The cooled solution was filtered and diluted with an equal volume of water. A yellow oil (1.89 g.) which separated and sank was drawn off from the separatory funnel. GLC indicated only myrtenyl methyl ether and unreacted myrtenyl chloride. The column was a 10-ft. by 1/4-in. 10%-Carbowax 20M column on a Varian A700 thermal conductivity instrument at 150°C. and 15 ml.min.$^{-1}$ helium. Preparative GLC on a 20-ft. by 3/8-in. Carbowax 20M column at 300 ml.min.$^{-1}$ helium and 150°C. on the same instrument gave 0.31 g. (15% recovery) of pure myrtenyl methyl ether. An NMR spectrum run on the collected myrtenyl methyl ether had signals very similar to those of myrtenyl chloride and myrtenol. Table IX gives the pertinent NMR signals.

trans-PINOCARVYL METHYL ETHER

The method of Kuhn, et al. (30) for methylation of a glucoside was followed. Barium oxide (18.4 g., 120 millimoles) and 5.0 g. trans-pinocarveol (35 millimoles) were stirred vigorously with 50 ml. distilled N,N-dimethylformamide while 15 ml. (33.2 g., 240 millimoles) methyl iodide were added slowly. Practically no temperature rise occurred so heat was applied until the reaction temperature rose to 73°C. Stirring was continued for another hour while 6 g. (40 millimoles) barium oxide and 5 ml. (80 millimoles) methyl iodide were added. The reaction solution was diluted with 600 ml. chloroform, filtered, washed with water, dried with Drierite and concentrated to give 4.9 g. of crude trans-pinocarvyl methyl ether. Fractional distillation at 5 mm. Hg gave 1.08 g. (6.4 millimoles, 19% of theory) of 90% pure trans-pinocarvyl methyl ether, b.p. 46-50°C., literature b.p.

TABLE IX

NMR SPECTRUM OF MYRTENYL METHYL ETHER[a]

Chemical Shift, α, p.p.m.	Integral Height, mm.	Number of Protons	J,Hz, and multiplicity[b]	Assignment[c]
5.50	10	1	1.5,M	Vinyl
3.88	21	2	1.5,Q	Methylene, α- to OMe and vinyl
3.28	33	3	S	Methoxyl
2.7-1.4	53	5	M	Other ring H's
1.28	32	3	S	Methyl, trans- to vinyl
1.17	10	1	8.3,D	One methylene H of cyclobutane ring, cis- to vinyl
0.85	29	3	S	Methyl, cis- to vinyl

[a] 60 MHz NMR spectrum run on a Varian A60A NMR spectrometer at normal probe temperature of 45°C. Concentration was 15% (v/v) in $CDCl_3$ with 1% tetramethylsilane internal standard.

[b] S = singlet, D = doublet, Q = quartet, M = multiplet.

[c] Reference (26).

57-60°C. at 6 mm. (12). The pertinent NMR signals are given in Table X. This spectrum was identical with the NMR spectrum of authentic trans-pinocarvyl methyl ether (12).

TABLE X

NMR SPECTRUM OF *trans*-PINOCARVYL METHYL ETHER[a]

Chemical Shift, α, p.p.m.	Integral Height, mm.	Number of Protons	J,Hz, and multiplicity[b]	Assignment[c]
4.90	19	2	S	Vinyl
3.80	10	1	6,D	Methine, α- to OMe and vinyl
3.32	31	3	S	Methoxyl
2.6-1.6	60	6	M	Other ring H
1.28	32	3	S	Methyl, *trans*- to OMe
0.68	30	3	S	Methyl, *cis*- to OMe

[a] 60 MHz NMR spectrum run on a Varian A60A NMR spectrometer at normal probe temperature of 45°C. Concentration was 15% (v/v) in $CDCl_3$ with 1% tetramethylsilane internal standard.

[b] S = singlet, D = doublet, M = multiplet.

[c] Reference (26).

METHODS

KINETIC TECHNIQUE

Equipment

A 10-l. stainless-steel bucket was equipped with a 0.5-amp. 1600-r.p.m. stirrer with two 1-in.-radius propellers on the shaft, and a rod to attach reaction vessels. Chloramine-T (10 p.p.m.) was used in the water to prevent slime growth. Temperature was maintained at 34.95 $\pm$ 0.03°C. by a 125-watt knife heater controlled by an electronic relay (Precision Scientific). Voltage to the heater was reduced to 75 v. by a Variac to evenly divide the cycle time (40 sec.) between heating and cooling. The temperature fluctuations were sufficiently rapid, and the half-lives of the reactions studied were long enough that the 0.06°C. temperature range could have no effect on the rate constants measured.

Elapsed reaction time was measured by an electric Reset Time Totalizer (Model C5D, Industrial Timer Corp.). The digital dials registered up to 9999.9 min. total before starting over again. This equipment made accurate measurement of long reaction times quite convenient.

Ten-ml. volumetric flasks and 15-ml. vials were used for kinetic and product analysis runs. They were soaked in and thoroughly brushed with hot Alkonox solution, then rinsed by soaking in hot tap water and in hot distilled water. After drying inverted at 110°C. overnight, they were rinsed three times with dry methanol and dried inverted in an evacuated desiccator over potassium hydroxide pellets overnight.

Reaction Procedure

The internal standard, 4-methoxytoluene (1 drop, about 20 mg.) was weighed in a 10-ml. volumetric flask. For methanolysis runs (neither sodium methoxide nor potassium acetate present) 2,6-dimethylpyridine (1 drop, about 20 mg.) and myrtenyl chloride (3 drops, about 40 mg.) were weighed in. The methanolic salt solution (for runs with added salts) was pipetted into the volumetric flask. It was then filled to the mark with dry methanol. The solution was shaken thoroughly to dissolve the organic liquids, poured into a 15-ml. vial, and a serum cap (Arthur H. Thomas Co.) was inserted in the vial neck to prevent entrance of atmospheric moisture and evaporation of methanol. The reacting solutions were placed in the bath at least one half-hour prior to taking the zero time sample. Duplicate reactions were prepared and sampled throughout the run. The same procedure was followed for runs with potassium acetate or sodium methoxide except that 2,6-dimethylpyridine was omitted.

At appropriate time intervals, reactions were sampled by withdrawing through the serum cap duplicate 0.2-ml. aliquots into a 0.5-ml. Microliter syringe (Hamilton Co.) fitted with a 3-in., 18-gage stainless-steel needle. Each aliquot was ejected into a 3-ml. test tube containing 1 ml. water and 1 ml. heptane. (This had been distilled to remove components with long GLC retention times.) Reactions buffered with 2,6-dimethylpyridine required 1 drop M hydrochloric acid in the aqueous phase of the extraction to wash the 2,6-dimethylpyridine from the heptane solution. This was desirable because the amine tailed badly on the GLC columns used. Reactions with potassium acetate required 1 drop of 5% aqueous sodium bicarbonate in the extraction to assure removal of acetic acid from the heptane solution. Acetic acid would also have tailed on the columns used, and it might have catalyzed rearrangement of the reactants and products in heptane

solution. Following vigorous shaking and phase separation, the heptane layer was dried over a potassium hydroxide pellet and stored in a 4-ml. vial with a Teflon-lined screw cap. These heptane solutions gave reproducible GLC relative Disc* integral ratios and no decrease in Disc integral response (for a given sample size) after standing at room temperature, exposed to light, as long as six months. Apparently, the unreacted myrtenyl chloride, the methyl ether and acetate products, and the internal standard, 4-methoxytoluene, were stable in heptane solution.

Aliquots of 2-7 μl. of these heptane solutions were analyzed by GLC to get Disc integral ratios for kinetic and product analysis calculations. The base-line-corrected Disc integral of each reactant and product peak was divided by the base-line-corrected Disc integral of the internal standard peak of each chromatogram. At least two chromatograms were run on one of the duplicate reaction samples for each time point. [Duplicates were taken as a safety measure. Statistical comparison of variances (19) showed that the variance between duplicate samples was less than the variance due to GLC analysis, 1% of the average Disc integral for any one peak.] All myrtenyl chloride concentration determinations were made by GLC on a 10-ft. by 1/8-in., 10%-Carbowax 20M column. Temperature was 100°C. nitrogen, carrier gas, flow rate was 20 $ml.min.^{-1}$ A 3-ft. by 1/8-in., 15%-β,β'-oxydipropionitrile column (ODPN) was operated at 75°C. and 15 $ml.min.^{-1}$ nitrogen, for trans-pinocarvyl chloride analysis. The Brown Model 16 recorder used was equipped with Model 227 Disc Chart Integrator with 60 r.p.m. motor.

*Disc Chart Integrator Model 227 manufactured by Disc Instruments, Inc., Santa Ana, Calif.

Calculations

The methanolysis (pseudo-first-order disappearance) rate constant for myrtenyl (or trans-pinocarvyl) chloride was calculated as the regression coefficient (19) of Naperian (natural or base e) logarithm (ln) of relative myrtenyl (or trans-pinocarvyl) chloride Disc integral on time. These calculations were done by an IBM 360-44 computer. It also plotted the ln (myrtenyl chloride/4-methoxytoluene) vs. time and mole fraction vs. time data given in the figures in Appendix III.

PRODUCT ANALYSIS

Qualitative

Myrtenyl methyl ether was identified by its NMR spectrum. The pertinent signals are listed in Table IX. trans-Pinocarvyl methyl ether and myrtenyl acetate were identified by comparison of relative GLC retention times on two different columns to authentic samples. Absence of trans-pinocarvyl acetate, and cis-pinocarvyl methyl ether were confirmed by finding no peak at the appropriate relative GLC retention times. Gruenewald (12) reported the retention time (relative to methoxybenzene) for cis-pinocarvyl methyl ether to be 0.77 on a 10-ft., 15%-ODPN column. Converted to retention time relative to myrtenyl methyl ether, cis-pinocarvyl methyl ether should appear at 1.15 on the ODPN column used for this work. No peak appeared at that relative retention time. The relative GLC retention times of cis-pinocarvyl acetate are not known. They are not, however, likely to be the same as one of the other acetates on two columns. No unidentifiable peaks were observed. The limit of detectability of any one product would be about 1% of the total reaction product. The relative GLC retention times of the expected products are given in Tables XI and XII.

TABLE XI

RELATIVE GLC RETENTION TIMES OF METHYL ETHERS[a]

Compound	Carbowax[b] 20M	ODPN[c]
Myrtenyl methyl ether	0.748	0.415
trans-Pinocarvyl methyl ether	0.662	0.346
4-Methoxytoluene	1.00[d]	1.00[e]

[a]The instrument was a Varian Aerograph 1200-1. H_2 flow to the FID was 30 ml.min.$^{-1}$ All retention times were corrected for the time lag between aliquot injection and solvent peak appearance.

[b]10% Carbowax 20M on 100-to 120-mesh Varaport 30 in a 10-ft. by 1/8-in. SS column.

[c]15% β,β'-oxydipropionitrile-(ODPN) on 100-to 120-mesh Varaport 30 in a 3-ft. by 1/8-in. SS column.

[d]Internal standard had retention time of 0.520 hr. at 100°C. and 20 ml.min.$^{-1}$ N_2.

[e]Internal standard had retention time of 0.600 hr. at 70°C. and 18 ml.min.$^{-1}$ N_2.

Quantitative

Substitution product yields and distributions were determined by quantitative GLC (31). The molar response factors used are listed in Appendix I. The data for their determination are also given there. The data for yield and product distribution calculations are given in Table XIV, Appendix II.

Response Factors

About 20 mg. (1 drop) of the internal standard (4-methoxytoluene) and the same for the compound were weighed into a 15-ml. vial and 10 ml. distilled heptane was added. At least five chromatograms were run on the column at the temperature and flow rate to be used for analysis of reaction products.

TABLE XII

RELATIVE GLC RETENTION TIMES OF ACETATES[a]

Compounds	Carbowax[b] 20M	SE30[c]
Myrtenyl acetate	3.32	4.9
trans-Pinocarvyl acetate	2.84	4.4
4-Methoxytoluene	1.00[d]	1.0[e]

[a]The instrument was a Varian Aerograph 1200-1. H_2 flow to the FID was 30 ml.min.$^{-1}$ All retention times were corrected for the time lag between aliquot injection and solvent peak appearance.

[b]10% Carbowax 20M on 100- to 120-mesh Varaport 30 in a 10-ft. by 1/8-in. SS column.

[c]5% SE30 on 60- to 80-mesh, acid washed, dichlorodimethylsilane-treated Chromosorb W in a 5-ft. by 1/8-in. SS column.

[d]Internal standard had retention time of 0.220 hr. at 125°C. and 20 ml.min.$^{-1}$ N_2.

[e]Internal standard had retention time of 2.6 min. at 90°C. plus 2°C. min.$^{-1}$ and 25 ml.min.$^{-1}$ N_2.

Yields

GLC determination of yields was done on the last kinetic sample taken. The methyl ether percentages were calculated from these data.

CONTROL EXPERIMENTS

MYRTENYL METHYL ETHER

This product was tested for stability under both acidic and basic conditions. Acid caused rapid loss of myrtenyl methyl ether and appearance of at least seven new components, according to GLC. Myrtenyl methyl ether was stable to basic conditions.

Methanolic hydrogen chloride, 0.1M, was prepared by reacting 0.28 ml. (0.4 millimole) acetyl chloride with 1 ml. dry methanol. To this was added 4 ml. 0.1M methanolic myrtenyl methyl ether. GLC indicated that only myrtenyl methyl ether (at 0.14 hr.) and materials with short retention times (methanol, methyl acetate and hydrogen chloride) were present. After ten days at 35°C. GLC of an 0.5-µl. aliquot gave peaks at the following retention times, in hours, with peak heights given as percentage of recorder scale: 0.09, 28; 0.14, 7; 0.16, 59; 0.20, 33; 0.26, 30; 0.37, 58; 0.46, 34; and 1.40, 28. The peak at 0.14 hr. was probably myrtenyl methyl ether. None of the other peaks had the same retention times as known compounds used in this study. The column had 10% 1,2,3-tris-(2-cyanoethoxy)-propane (TCEP) coated on 70-to 80-mesh, acid-washed, dichlorodimethylsilane-treated Chromosorb-G packed in a 10-ft. by 1/8-in. SS column. Temperature was 110°C., and flow rate was 40 p.s.i. nitrogen on the 1200-1 chromatograph.

To evaluate the stability of myrtenyl methyl ether — especially toward allylic rearrangement — under basic conditions, 182 mg. (1.10 millimoles) myrtenyl methyl ether, 131 mg. (1.07 millimoles) 4-methoxytoluene, and 1.0 ml. 2.0M methanolic sodium hydroxide were diluted to 10 ml. in a clean vial (see kinetics section).

The initial mole ratio was 1.03. After thirteen days at 35°C. the GLC area ratio was 1.325 ± 0.004. The mole ratio was 0.985 ± 0.003. Recovery was 96%.

No new peaks were observed. Temperature of the TCEP column was 110°C., and nitrogen flow was 40 ml.min.$^{-1}$ on the 1200-1. Peak areas were measured by a Technicon model AAG integrator.

To check the stability of myrtenyl methyl ether toward 2,6-dimethylpyridine in methanol, 291 mg. (1.75 millimoles) myrtenyl methyl ether, 184 mg. (151 millimoles) 4-methoxytoluene, and 337 mg. (3.15 millimoles) 2,6-dimethylpyridine were diluted to about 15 ml. with dry methanol. The vial was closed with a teflon-lined screw cap and kept at 35°C. for thirteen days. GLC before and after gave area ratios of 1.478 and 1.494, respectively. The recovery was apparently 101%. No new peaks were observed after reaction. The column was 5-ft. of 20% Carbowax 20MTPA. Temperature was 100°C. and nitrogen flow was 20 ml.min.$^{-1}$ on the 1200-1. Two chromatograms were run for each sample. Peak areas were measured by the Technicon integrator.

trans-PINOCARVYL METHYL ETHER

This product (0.017M) was exposed to 0.02M 2,6-dimethylpyridine and 0.02M 2,6-dimethylpyridine hydrochloride together in methanol for seven days at 35°C. The reaction was sampled and worked up in the manner used for kinetic work. Disc integral ratios before and after were 1.193 and 1.222, respectively. The apparent recovery was 102%. No new peaks were observed after reaction. GLC equipment and conditions were the same as for kinetic runs. The Disc integral ratios are averages of three chromatograms.

MYRTENYL ACETATE

This product (0.022M) was reacted with 0.3M potassium acetate, 0.02M acetic acid, and 0.02M sodium chloride together in dry methanol for seven days at 35°C. Aliquots were worked up by the kinetic technique. Three chromatograms were run on the Carbowax 20M column used for kinetics at 100°C. + 1°C, min.$^{-1}$ and 15 ml.min.$^{-1}$ nitrogen. The average Disc integral ratios before and after were 1.176 ± 0.062 and 1.110 ± 0.009, respectively. Recovery was apparently 93.5 ± 3.0%. The only new GLC peak after reaction had the same relative retention time as authentic myrtenol (5.22 times that for 4-methoxytoluene). An approximate pseudo-first-order rate constant for disappearance of myrtenyl acetate was calculated from

$$k = -\ln 0.935/(6.05 \times 10^5 \text{ sec.}) \qquad (17)$$

The result is $0.067/6.55 \times 10^5 = 1.1 \times 10^{-7}$ sec.$^{-1}$ The Disc integral ratio for myrtenol was 0.042. The difference between initial and final myrtenyl acetate Disc integral ratios is 0.066, which is barely larger than σ, 0.062. When converted to mole ratios, the unrecovered myrtenyl acetate was 0.042 ± 0.040, and the myrtenol appearing was ± 0.030 (σ was less than 0.001). Within experimental error, myrtenol accounts for the myrtenyl acetate which disappeared.

trans-PINOCARVYL ACETATE

This product (0.016M) was subjected to the same treatment as myrtenyl acetate. Disc integral ratios were 1.115 ± 0.026 before and 1.126 ± 0.036 after seven days at 35.0°C. Recovery was apparently 101 ± 3%. GLC showed no new peaks after reaction.

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APPENDIX I

DETERMINATION OF RESPONSE FACTORS

4-Methoxytoluene (22.7 mg., 0.186 millimole) and 41.5 mg. (0.243 millimole) myrtenyl chloride were put in a 15-ml. vial with 10 ml. distilled heptane. GLC runs were made on the columns used for qualitative and quantitative analyses. The mole ratio of myrtenyl chloride to 4-methoxytoluene in the standard solution (1.31), was adjusted for the trans-pinocarvyl chloride present by assuming the same response factor for both. Myrtenyl chloride was 95.9% of the sum of Disc integrals for the two peaks. Thus, the true mole ratio of myrtenyl chloride in the standard solution was 0.959 x 1.31 = 1.26. When this was divided by the average of five Disc integral ratios (1.70) a response factor of 0.741 resulted.

The response factor for trans-pinocarvyl chloride was determined on an impure sample. The ratio of trans-pinocarvyl to myrtenyl chloride was 0.28:1.16. The known weight of chlorides (43.5 mg., 0.254 millimole) and 4-methoxytoluene (20.9 mg., 0.171 millimole) were used to calculate a mole ratio (1.49). The Disc integrals of the GLC peaks and the response factor of myrtenyl chloride (see above) were used to calculate the mole ratio of myrtenyl chloride present (1.16). It was subtracted from 1.49 to get the approximate mole ratio of everything else present (0.33). Of this, 85% was trans-pinocarvyl chloride and 15% was trans-pinocarveol. Thus, the true mole fraction of trans-pinocarvyl chloride was 0.33 x 0.85 = 0.28. The response factor is thus 0.28/0.36 = 0.78.

The procedure used for myrtenyl chloride was applied to myrtenyl methyl ether (98%, 2% trans-pinocarvyl methyl ether), to trans-pinocarvyl methyl ether (95%, 5% myrtenyl methyl ether and trans-pinocarveol), to myrtenyl acetate (99%) and to myrtenol (99%). Table XIII gives the weights, average Disc integral ratios and calculated results.

TABLE XIII

RESPONSE FACTORS

Compound	Weight, mg.		Apparent Mole Ratio	Average Disc Integral Ratio		Purity, % of total integral	Mole Response	
	Compound	Internal Standard[a]		Compound	Impurities		Factor	SE(R)
Myrtenyl chloride	41.5	22.7	1.31	1.698	0.073	95.9	0.741	0.007
trans-Pinocarvyl chloride[b]	15.7	20.9	0.33	0.362	0.064	85.0	0.78	0.015
Myrtenyl methyl ether	29.1	18.4	1.16	1.529	0.0364	97.6	0.743	0.007
trans-Pinocarvyl methyl ether	23.4	14.9	1.16	1.576	0.0823	95.2	0.700	0.007
Myrtenyl acetate	26.8	22.1	0.763	1.174	0.013	98.9	0.642	0.007
Myrtenol	28.8	24.6	0.940	1.278	0.019	98.5	0.642	0.008

[a] 4-Methoxytoluene.

[b] About 20% of total chloride present. These numbers are corrected for myrtenyl chloride determined by GLC.

An estimate of the errors in the response factors can be made by applying the formula (19) for the variance of a linear function of variables to the calculation of the response factors from area ratios (or 1%) and mole ratios (assumed to be exact to three significant figures). The result is that the standard error of the response factors [SE(R)] is not greater than 1% of the response factor.

APPENDIX II

YIELD DATA FOR MYRTENYL CHLORIDE

The yield data given in this appendix were obtained from the last kinetic sample for each run. The internal standard (4-methoxytoluene) was already present in the methanolic reaction solution. The work-up procedure is described in the experimental section.

TABLE XIV

INITIAL MOLE RATIO OF MyCl

Salt or Nucleophile	Weights, mg.			Mole Radius		Concentrations, MXLOO	
	MyCl[a]	Mean[b]	DMP[c]	MyCl / Mean	DMP / MyCl	MyCl	DMP
No salt	44.7	23.5	38.3	1.35	1.37	2.61	3.58
No salt	44.3	22.4	26.0	1.41	0.939	2.59	2.43
No salt	44.8	22.2	24.2	1.44	0.846	2.62	2.26
No salt	45.6	23.1	23.0	1.40	0.807	2.62	2.15
No salt	37.3	23.3	23.8	1.14	1.02	2.18	2.22
No salt	38.3	21.9	21.5	1.25	0.898	2.24	2.01
0.02M NaOMe + 0.03M $LiClO_4$	20.4	12.0	0	1.21	0	1.19	0
0.02M NaOMe + 0.03M $LiClO_4$	22.8	9.0	0	1.80	0	1.33	0
0.035M NaOMe + 0.015M $LiClO_4$	21.5	22.2	0	0.690	0	1.26	0
0.035M NaOMe + 0.015M $LiClO_4$	23.1	21.5	0	0.763	0	1.35	0
0.05M $LiClO_4$	22.9	21.1	18.8	0.777	1.31	1.34	1.76
0.05M $LiClO_4$	23.1	23.3	24.6	0.707	1.70	1.35	2.30
0.05M LiCl	43.5	27.0	24.2	1.15	0.890	2.54	2.26
0.05M LiCl	42.5	25.0	25.9	1.21	0.975	2.49	2.42
0.3M KOAc	44.1	15.0	0	2.10	0	2.58	0
0.3M KOAc	53.2	20.3	0	1.87	0	3.11	0

[a] Myrtenyl chloride.

[b] 4-Methoxytoluene.

[c] 2,6-Dimethylpyridine.

TABLE XV

YIELD DATA FOR MYRTENYL CHLORIDE[a]

Salt or Nucleophile	% MyCl Remaining	Final Mole Ratios			Sum of Final Mole Ratios	Initial Mole Ratio[e]	Yield, % of theory[f]
		MyCl[b]	MyOMe[c]	PiOMe[d]			
No salt[i]	1.3	0.174	1.07	0.178	1.42	1.35	105
No salt	1.2	0.175	1.08	0.180	1.44	1.41	102
No salt	0	0	0.925	0.155	1.08	1.14	94.7
No salt	0	0	1.019	0.170	1.19	1.25	95.2
0.02M NaOMe + 0.03M $LiClO_4$	4.8	0.058	0.976	0.132	1.17	1.21	96.7
0.02M NaOMe + 0.03M $LiClO_4$	1.2	0.022	1.520	0.211	1.75	1.80	97.2
0.035M NaOMe + 0.015M $LiClO_4$	5.1	0.035	0.570	0.055	0.660	0.690	95.7
0.035M NaOMe + 0.015M $LiClO_4$	5.2	0.040	0.623	0.060	0.723	0.763	94.8
0.05M $LiClO_4$	10	0.079	0.625	0.092	0.796	0.777	102
0.05M $LiClO_4$	9.8	0.070	0.550	0.082	0.702	0.707	99.3
0.05M LiCl	1.2	0.142	0.862	0.144	1.15	1.15	100
0.05M LiCl	1.2	0.144	0.862	0.146	1.15	1.21	95.0
No salt[j]	0	0	1.224	0.159	1.38	1.44	95.8
No salt	0	0	1.154	0.151	1.31	1.40	93.6
0.3M KOAc	7.5	0.157	1.276	0.151	2.12[g]	2.10	101
0.3M KOAc	7.4	0.139	1.104	0.127	1.80[h]	1.87	101

[a] Temperature was 35.0°C. Final mole ratios were obtained from average Disc integral ratio times the response factor for each compound. Runs without NaOMe or KOAc were buffered with 0.02-0.03M 2,6-dimethylpyridine.

[b] Myrtenyl chloride.

[c] Myrtenyl methyl ether.

[d] trans-Pinocarvyl methyl ether.

[e] By weight from Table XIV.

[f] The average yield was 98.1 ± 3.4%.

[g] Includes mole ratio of myrtenyl acetate of 0.539. Myrtenyl acetate was 25.4% of total products.

[h] Includes mole ratio of myrtenyl acetate of 0.507. Myrtenyl acetate was 27.0% of total products.

[i] GLC indicated that 20% of the starting chloride was trans-pinocarvyl.

[j] GLC indicated that 4% of the starting chloride was trans-pinocarvyl.

APPENDIX III

KINETIC DATA FOR MYRTENYL AND *trans*-PINOCARVYL CHLORIDES

All runs were made in the same bath at 35.0°C. Runs without sodium methoxide or potassium acetate were buffered with 2,6-dimethylpyridine. The extraction procedure described in the experimental section was used for all runs except Run 72, which was analyzed directly on the same instrument and column. Initial myrtenyl chloride concentration was 0.01-0.03M for all runs. Calculations in the ln (C_o/C) and mole fraction columns used the calculated initial concentration obtained as the antilog of the intercept of the least-squares regression of ln (myrtenyl chloride/4-methoxytoluene) against time.

TABLE XVI

KINETIC DATA FOR MyCl, RUN 118

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.678	1.9690	0.2838E-01	1.0288	1
649	0.528	1.6960	0.1209E 00	0.8861	2
1452	0.332	1.3940	0.3170E 00	0.7284	3
1920	0.325	1.3840	0.3242E 00	0.7231	4
2607	0.119	1.1260	0.5305E 00	0.5883	5
3337	0.053	1.0540	0.5966E 00	0.5507	6
4186	-0.155	0.8567	0.8038E 00	0.4476	7
5545	-0.403	0.6680	0.1053E 01	0.3490	8
7057	-0.651	0.5216	0.1300E 01	0.2725	9
9294	-1.097	0.3340	0.1746E 01	0.1745	10

Rate, $sec.^{-1}$	Sigma	Variance
5.1269E-06	5.8488E-08	3.4209E-15

TABLE XVII

KINETIC DATA FOR MyCl, RUN 120

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.584	1.7930	0.1685E-01	0.9833	1
650	0.458	1.5810	0.1427E 00	0.8670	2
1453	0.338	1.4020	0.2628E 00	0.7689	3
1921	0.268	1.3070	0.3330E 00	0.7168	4
2610	0.105	1.1110	0.4955E 00	0.6093	5
3338	0.049	1.0500	0.5519E 00	0.5758	6
-189	-0.111	0.8952	0.7114E 00	0.4908	7
5546	-0.394	0.6741	0.9951E 00	0.3697	8
7059	-0.689	0.5023	0.1289E 01	0.2755	9
9293	-1.088	0.3370	0.1688E 01	0.1848	10

Rate, $sec.^{-1}$	Sigma	Variance
2.9983E-06	5.3888E-08	2.9039E-15

TABLE XVIII

KINETIC DATA FOR MyCl, RUN 122

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.202	1.2240	0.2782E-02	0.9972	1
151	0.135	1.1450	0.6950E-01	0.9329	2
452	0.135	1.1450	0.6950E-01	0.9329	3
651	0.112	1.1190	0.9247E-01	0.9117	4
1453	-0.042	0.9592	0.2466E 00	0.7815	5
1921	-0.137	0.8719	0.3420E 00	0.7104	6
2613	-0.250	0.7788	0.4549E 00	0.6345	7
3341	-0.386	0.6795	0.5913E 00	0.5536	8
4191	-0.555	0.5739	0.7602E 00	0.4676	9
5546	-0.803	0.4479	0.1008E 01	0.3649	10
7061	-1.051	0.3496	0.1256E 01	0.2848	11
9292	-1.452	0.2340	0.1657E 01	0.1906	12

Rate, $sec.^{-1}$	Sigma	Variance
2.9771E-06	3.0881E-08	9.5362E-16

TABLE XIX

KINETIC DATA FOR MyCl, RUN 124

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.283	1.3270	0.2737E-02	0.9973	1
151	0.246	1.2790	0.3958E-01	0.9612	2
451	0.224	1.2510	0.6172E-01	0.9402	3
652	0.173	1.1890	0.1125E 00	0.8936	4
1102	0.082	1.0850	0.2041E 00	0.8154	5
1453	0.005	1.0050	0.2807E 00	0.7553	6
1921	-0.079	0.9245	0.3642E 00	0.6948	7
2614	-0.193	0.8242	0.4790E 00	0.6194	8
3342	-0.342	0.7101	0.6280E 00	0.5337	9
4191	-0.520	0.5943	0.8060E 00	0.4466	10
7056	-1.110	0.3294	0.1396E 01	0.2476	11
9292	-1.413	0.2434	0.1699E 01	0.1829	12

Rate, $sec.^{-1}$	Sigma	Variance
3.1411E-06	5.0296E-08	2.5297E-15

TABLE XX

KINETIC DATA FOR MyCl + 0.05M $LiClO_4$, RUN 90

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	-0.337	0.7140	0.3512E-01	1.0357	1
722	-0.499	0.6070	0.1272E 00	0.8805	2
1439	-0.650	0.5220	0.2781E 00	0.7572	3
2160	-0.781	0.4580	0.4089E 00	0.6644	4
2872	-0.919	0.3990	0.5468E 00	0.5788	5
4626	-1.317	0.2680	0.9448E 00	0.3888	6
5799	-1.470	0.2300	0.1098E 01	0.3336	7
7243	-1.796	0.1660	0.1424E 01	0.2408	8
8674	-2.017	0.1330	0.1645E 01	0.1929	9
10075	-2.235	0.1070	0.1863E 01	0.1552	10

Rate, $sec.^{-1}$	Sigma	Variance
3.1708E-06	5.8001E-08	3.3641E-15

TABLE XXI

KINETIC DATA FOR MyCl + 0.05M $LiClO_4$, RUN 92

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	-0.451	0.6370	0.2224E-01	1.0225	1
716	-0.607	0.5450	0.1337E 00	0.8748	2
1435	-0.753	0.4710	0.2797E 00	0.7560	3
2155	-0.889	0.4110	0.4159E 00	0.6597	4
2893	-1.036	0.3530	0.5624E 00	0.5698	5
4621	-1.363	0.2560	0.8893E 00	0.4109	6
5796	-1.575	0.2070	0.1102E 01	0.3323	7
7236	-1.917	0.1470	0.1444E 01	0.2360	8
8665	-2.129	0.1190	0.1655E 01	0.1910	9
10069	-2.367	0.0938	0.1893E 01	0.1506	10

Rate, $sec.^{-1}$	Sigma	Variance
3.1943E-06	4.1159E-08	1.6941E-15

TABLE XXII

KINETIC DATA FOR MyCl + 0.02M NaOMe + 0.03M $LiClO_4$, RUN 76

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.208	1.2310	0.7683E-01	1.0799	1
200	0.117	1.1240	0.1411E-01	0.9860	2
400	0.071	1.0740	0.5961E-01	0.9421	3
600	0.026	1.0260	0.1053E 00	0.9000	4
800	-0.053	0.9483	0.1841E 00	0.8319	5
1000	-0.101	0.9036	0.2324E 00	0.7927	6
1200	-0.197	0.8211	0.3281E 00	0.7203	7
1600	-0.394	0.6746	0.5246E 00	0.5918	8
2000	-0.451	0.6370	0.5820E 00	0.5588	9
2600	-0.695	0.4992	0.8257E 00	0.4379	10
3000	-0.762	0.4667	0.8931E 00	0.4094	11
3600	-0.919	0.3991	0.1050E 01	0.3501	12
4104	-0.996	0.3693	0.1127E 01	0 3240	13
4492	-1.232	0.2916	0.1363E 01	0.2558	14
4900	-1.309	0.2702	0.1440E 01	0.2370	15
8979	-2.360	0.0944	0.2491E 01	0.0828	16
9342	-2.412	0.0896	0.2543E 01	0.0786	17
9847	-2.545	0.0785	0.2676E 01	0.0689	18

Rate, $sec.^{-1}$	Sigma	Variance
4.6484E-06	8.1803E-08	6.6918E-15

TABLE XXIII

KINETIC DATA FOR MyCl + 0.02M NaOMe + 0.03M $LiClO_4$, RUN 77

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.543	1.7210	0.1834E-01	0.9818	1
1000	0.249	1.2830	0.3120E 00	0.7319	2
2000	-0.030	0.9704	0.5913E 00	0.5536	3
3007	-0.319	0.7217	0.8799E 00	0.4148	4
4000	-0.607	0.5451	0.1168E 01	0.3110	5
5000	-0.804	0.4477	0.1365E 01	0.2554	6
5975	-1.055	0.3482	0.1616E 01	0.1986	7
6962	-1.317	0.2679	0.1878E 01	0.1528	8
9010	-1.889	0.1512	0.2450E 01	0.0863	9
14100	-3.507	0.0300	0.4068E 01	0.0171	10

Rate, $sec.^{-1}$	Sigma	Variance
4.6837E-06	8.7229E-08	7.6089E-15

TABLE XXIV

KINETIC DATA FOR MyCl + 0.035M NaOMe + 0.015M $LiClO_4$, RUN 94

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	-0.691	0.5010	0.1868E-02	0.9981	1
711	-0.919	0.3990	0.2295E 00	0.7949	2
1431	-1.097	0.3340	0.4073E 00	0.6654	3
2156	-1.423	0.2410	0.7337E 00	0.4801	4
2890	-1.687	0.1850	0.9981E 00	0.3686	5
4616	-2.226	0.1080	0.1536E 01	0.2152	6
7228	-3.041	0.0478	0.2351E 01	0.0952	7

Rate, $sec.^{-1}$	Sigma	Variance
5.4805E-06	1.0839E-07	1.1749E-14

TABLE XXV

KINETIC DATA FOR MyCl + 0.035M NaOMe + 0.015M $LiClO_4$, RUN 96

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	-0.545	0.5800	0.4607E-01	1.0471	1
703	-0.792	0.4530	0.2011E 00	0.8179	2
1427	-1.058	0.3470	0.4676E 00	0.6265	3
2150	-1.339	0.2620	0.7486E 00	0.4730	4
2885	-1.609	0.2000	0.1019E 01	0.3611	5
4613	-2.120	0.1200	0.1529E 01	0.2167	6
7221	-2.922	0.0538	0.2332E 01	0.0971	7

Rate, $sec.^{-1}$	Sigma	Variance
5.4837E-06	1.3159E-07	1.7315E-14

TABLE XXVI

KINETIC DATA FOR MyCl + 0.05M NaOMe, RUN 72[a]

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	-0.675	0.5090	0.3270E-01	0.9678	1
32	-0.644	0.5250	0.1750E-02	0.9983	2
64	-0.679	0.5070	0.3664E-01	0.9640	3
96	-0.685	0.5040	0.4257E-01	0.9583	4
128	-0.681	0.5060	0.3861E-01	0.9621	5
160	-0.703	0.4950	0.6059E-01	0.9412	6
192	-0.719	0.4870	0.7688E-01	0.9260	7
224	-0.719	0.4870	0.7688E-01	0.9260	8
256	-0.738	0.4780	0.9554E-01	0.9089	9
288	-0.749	0.4730	0.1061E 00	0.8994	10
352	-0.783	0.4570	0.1405E 00	0.8690	11
400	-0.837	0.4330	0.1944E 00	0.8233	12
500	-0.863	0.4220	0.2201E 00	0.8024	13
553	-0.899	0.4070	0.2563E 00	0.7739	14
650	-0.921	0.3980	0.2787E 00	0.7568	15
700	-0.919	0.3990	0.2762E 00	0.7587	16
800	-0.981	0.3750	0.3382E 00	0.7130	17
1000	-1.073	0.3420	0.4303E 00	0.6503	18
1400	-1.252	0.2860	0.6092E 00	0.5438	19
1600	-1.328	0.2650	0.6854E 00	0.5039	20
1800	-1.406	0.2450	0.7639E 00	0.4659	21
2100	-1.514	0.2200	0.8715E 00	0.4183	22

Rate, $sec.^{-1}$	Sigma	Variance
7.0615E-06	9.2130E-08	8.4880E-15

[a]This run was analyzed by direct injection of 20-µl. aliquots on the Carbowax 20M column previously described.

TABLE XXVII

KINETIC DATA FOR MyCl + 0.05M NaOMe, RUN 73

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.124	1.1320	0.1049E 00	1.1106	1
50	0.050	1.0510	0.3061E-01	1.0311	2
100	0.031	1.0310	0.1140E-01	1.0115	3
200	-0.015	0.9850	0.3424E-01	0.9663	4
250	-0.065	0.9370	0.8420E-01	0.9192	5
310	-0.083	0.9200	0.1025E 00	0.9026	6
400	-0.211	0.8100	0.2298E 00	0.7947	7
700	-0.331	0.7180	0.3504E 00	0.7044	8
1000	-0.423	0.6550	0.4422E 00	0.6426	9
1200	-0.550	0.5770	0.5690E 00	0.5661	10
1401	-0.622	0.5370	0.6409E 00	0.5268	11
1650	-0.730	0.4820	0.7489E 00	0.4729	12
1800	-0.814	0.4430	0.8333E 00	0.4366	13
1801	-0.803	0.4480	0.8221E 00	0.4395	14
2430	-1.064	0.3450	0.1083E 01	0.3385	15
2800	-1.178	0.3080	0.1197E 01	0.3022	16
3210	-1.343	0.2610	0.1362E 01	0.2561	17
3900	-1.590	0.2040	0.1609E 01	0.2001	18
4440	-1.778	0.1690	0.1797E 01	0.1658	19

Rate, $sec.^{-1}$	Sigma	Variance
7.0901E-06	1.6590E-07	2.7524E-14

TABLE XXVIII

KINETIC DATA FOR MyCl + 0.3M KOAc, RUN 140

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	1.044	2.8400	0.9852E-02	1.0099	1
506	0.883	2.4180	0.1510E 00	0.8598	2
506	0.870	2.3860	0.1643E 00	0.8485	3
1100	0.691	1.9960	0.3428E 00	0.7098	4
1100	0.700	2.0130	0.3343E 00	0.7158	5
1793	0.480	1.6160	0.5540E 00	0.5746	6
2629	0.214	1.2390	0.8196E 00	0.4406	7
3381	-0.037	0.9635	0.1071E 01	0.3426	8
4611	-0.398	0.6716	0.1432E 01	0.2388	9
6051	-0.856	0.4248	0.1890E 01	0.1511	10
8210	-1.551	0.2120	0.2585E 01	0.0754	11
11800	-2.619	0.0729	0.3653E 01	0.0259	12

Rate, $sec.^{-1}$	Sigma	Variance
5.1924E-06	1.9340E-08	3.7405E-16

TABLE XXIX

KINETIC DATA FOR MyCl + 0.3M KOAc, RUN 142

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.821	2.2720	0.2519E-01	1.0255	1
506	0.660	1.9350	0.1354E 00	0.8734	2
1100	0.457	1.5790	0.3387E 00	0.7127	3
1100	0.456	1.5780	0.3393E 00	0.7123	4
1794	0.252	1.2870	0.5432E 00	0.5809	5
1794	0.248	1.2820	0.5470E 00	0.5787	6
2629	-0.017	0.9830	0.8126E 00	0.4437	7
2629	-0.024	0.9762	0.8196E 00	0.4406	8
3382	-0.282	0.7540	0.1078E 01	0.3403	9
3382	-0.279	0.7563	0.1075E 01	0.3414	10
4611	-0.671	0.5113	0.1466E 01	0.2308	11
4611	-0.677	0.5083	0.1472E 01	0.2294	12
6051	-0.999	0.3682	0.1795E 01	0.1662	13
8210	-1.671	0.1880	0.2467E 01	0.0849	14
11800	-2.870	0.0567	0.3665E 01	0.0256	15

Rate, $sec.^{-1}$	Sigma	Variance
5.1395E-06	5.2435E-08	2.7495E-15

TABLE XXX

KINETIC DATA FOR MyCl + 0.05M LiCl, RUN 102

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.191	1.2100	0.4304E-01	1.0440	1
821	0.020	1.0200	0.1278E 00	0.8800	2
1462	-0.124	0.8830	0.2720E 00	0.7618	3
2218	-0.273	0.7610	0.4207E 00	0.6566	4
3004	-0.422	0.6560	0.5692E 00	0.5660	5
4263	-0.669	0.5120	0.8170E 00	0.4418	6
5712	-0.892	0.4100	0.1039E 01	0.3537	7
7318	-1.168	0.3110	0.1316E 01	0.2683	8
10053	-1.650	0.1920	0.1798E 01	0.1657	9

Rate, $sec.^{-1}$	Sigma	Variance
3.0206E-06	5.2214E-08	2.7263E-15

TABLE XXXI

KINETIC DATA FOR MyCl + 0.05M LiCl, RUN 104

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.191	1.2100	0.3684E-01	1.0375	1
818	0.030	1.0300	0.1242E 00	0.8832	2
1460	-0.123	0.8840	0.2771E 00	0.7580	3
2216	-0.257	0.7730	0.4113E 00	0.6628	4
3001	-0.419	0.6580	0.5723E 00	0.5642	5
4263	-0.639	0.5280	0.7924E 00	0.4527	6
5711	-0.892	0.4100	0.1045E 01	0.3516	7
7315	-1.171	0.3100	0.1325E 01	0.2658	8
10051	-1.635	0.1950	0.1789E 01	0.1672	9

Rate, $sec.^{-1}$	Sigma	Variance
3.0139E-06	4.5502E-08	2.0704E-15

TABLE XXXII

KINETIC DATA FOR PiCl, RUN 122[a]

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	-1.884	0.1520	0.2182E-01	1.0221	1
151	-1.981	0.1380	0.7481E-01	0.9279	2
452	-2.354	0.0950	0.4482E 00	0.6388	3
1453	-3.338	0.0355	0.1433E 01	0.2387	4
1924	-3.689	0.0250	0.1783E 01	0.1681	5
651	-2.628	0.0722	0.7226E 00	0.4855	6

Rate, $sec.^{-1}$	Sigma	Variance
1.5978E-05	7.0387E-07	4.9543E-13

[a]This GLC analysis was done on the ODPN column.

TABLE XXXIII

KINETIC DATA FOR PiCl, RUN 124[a]

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
151	-1.904	0.1490	0.4562E-01	0.9554	1
451	-2.303	0.1000	0.4444E 00	0.6412	2
652	-2.399	0.0908	0.5409E 00	0.5822	3
1102	-2.921	0.0539	0.1062E 01	0.3456	4
1453	-3.106	0.0448	0.1247E 01	0.2873	5
1921	-3.448	0.0318	0.1590E 01	0.2039	6

Rate, $sec.^{-1}$	Sigma	Variance
1.4342E-05	9.3589E-07	8.7589E-13

[a]This GLC analysis was done on the ODPN column.

TABLE XXXIV

KINETIC DATA FOR MyCl, RUN 122[a]

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.254	1.2890	0.6290E-02	0.9937	1
151	0.200	1.2210	0.6049E-01	0.9413	2
452	0.186	1.2040	0.7451E-01	0.9282	3
651	0.198	1.2190	0.6213E-01	0.9398	4
1453	0.050	1.0510	0.2104E 00	0.8102	5
1921	-0.032	0.9687	0.2920E 00	0.7468	6
2613	-0.339	0.7123	0.5994E 00	0.5491	7
3341	-0.373	0.6884	0.6335E 00	0.5307	8
4191	-0.601	0.5480	0.8616E 00	0.4225	9
5546	-0.677	0.5080	0.9374E 00	0.3916	10
7061	-1.016	0.3620	0.1276E 01	0.2791	11
9292	-1.442	0.2365	0.1702E 01	0.1823	12

Rate, $sec.^{-1}$	Sigma	Variance
3.0523E-06	1.0904E-07	1.1890E-14

[a]This GLC analysis was done on the ODPN column.

TABLE XXXV

KINETIC DATA FOR MyCl, RUN 124[a]

Time, min.	ln(RCl/Mean)	RCl/Mean	$\ln(C_o/C)$	Mole Fraction	
0	0.325	1.3840	0.3449E-01	0.9661	1
151	0.285	1.3300	0.7429E-01	0.9284	2
451	0.311	1.3650	0.4831E-01	0.9528	3
652	0.218	1.2430	0.1419E 00	0.8677	4
1102	0.156	1.1690	0.2033E 00	0.8160	5
1453	0.079	1.0820	0.2807E 00	0.7553	6
1921	-0.028	0.9722	0.3877E 00	0.6786	7
2614	-0.091	0.9126	0.4509E 00	0.6370	8
3342	-0.192	0.8256	0.5511E 00	0.5763	9
4191	-0.447	0.6394	0.8067E 00	0.4463	10
5546	-0.657	0.5186	0.1016E 01	0.3620	11
7070	-1.076	0.3409	0.1436E 01	0.2380	12
9292	-1.396	0.2475	0.1756E 01	0.1728	13

Rate, $sec.^{-1}$	Sigma	Variance
3.1701E-06	7.8986E-08	6.2388E-15

[a]This GLC analysis was done on the ODPN column.

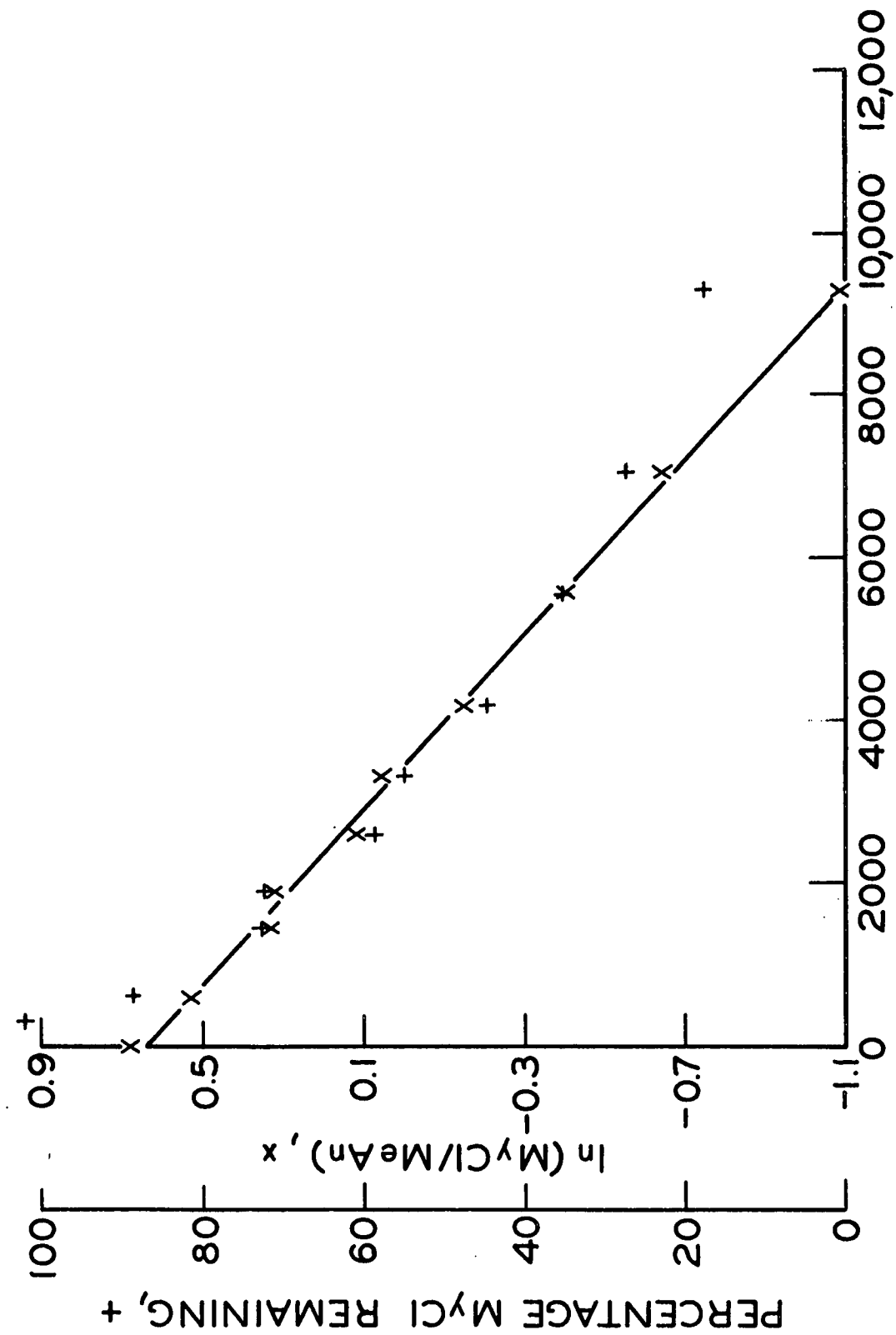

Figure 5. Plot of Percentage Myrtenyl Chloride Remaining, +, and ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(3.31 \pm 0.06) \times 10^{-4}$ sec.$^{-1}$. This Reaction was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 118

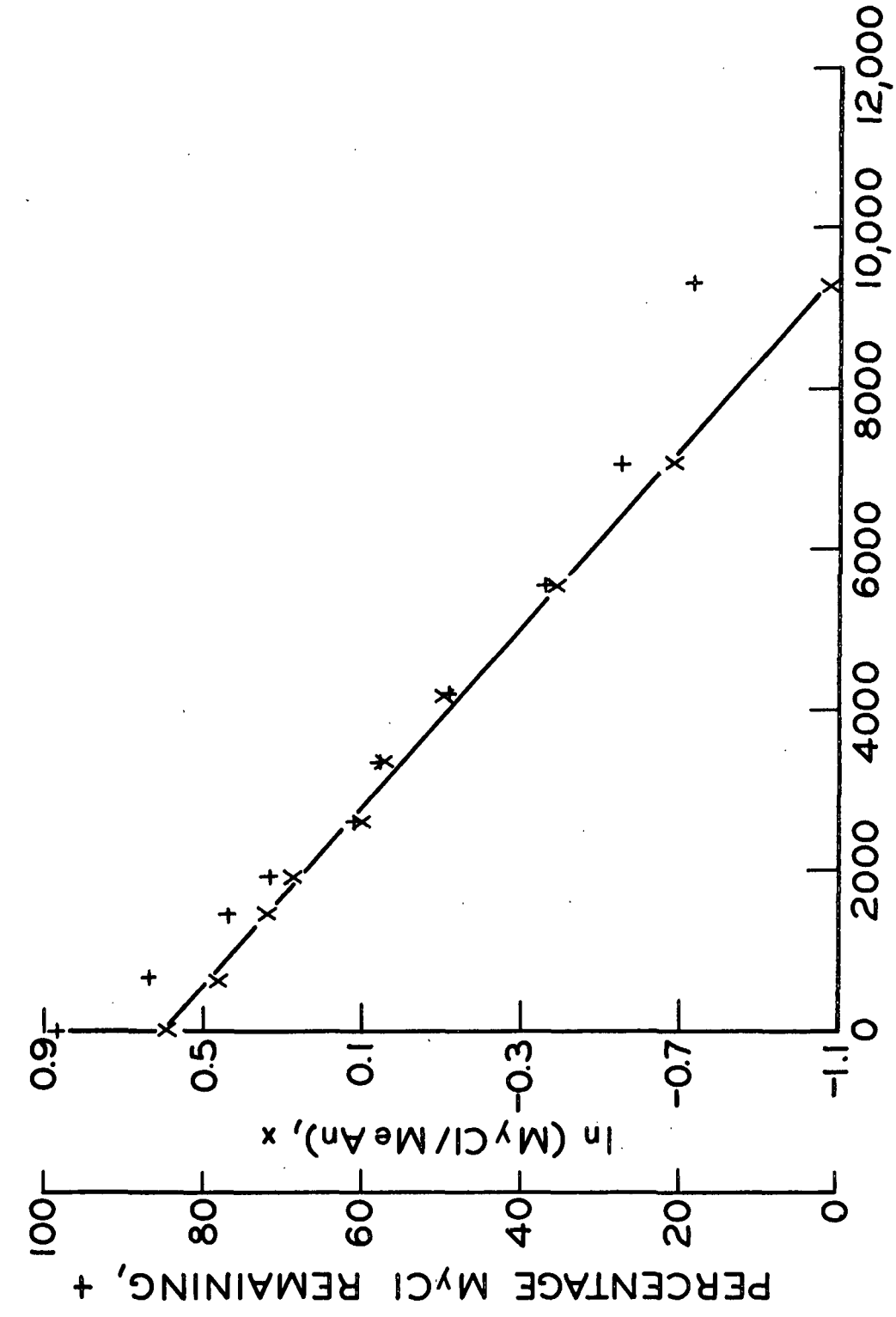

Figure 6. Plot of Percentage Myrtenyl Chloride Remaining, +, and ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, (3.00 ± 0.05) x 10^{-6} sec.$^{-1}$. This Reaction was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 120

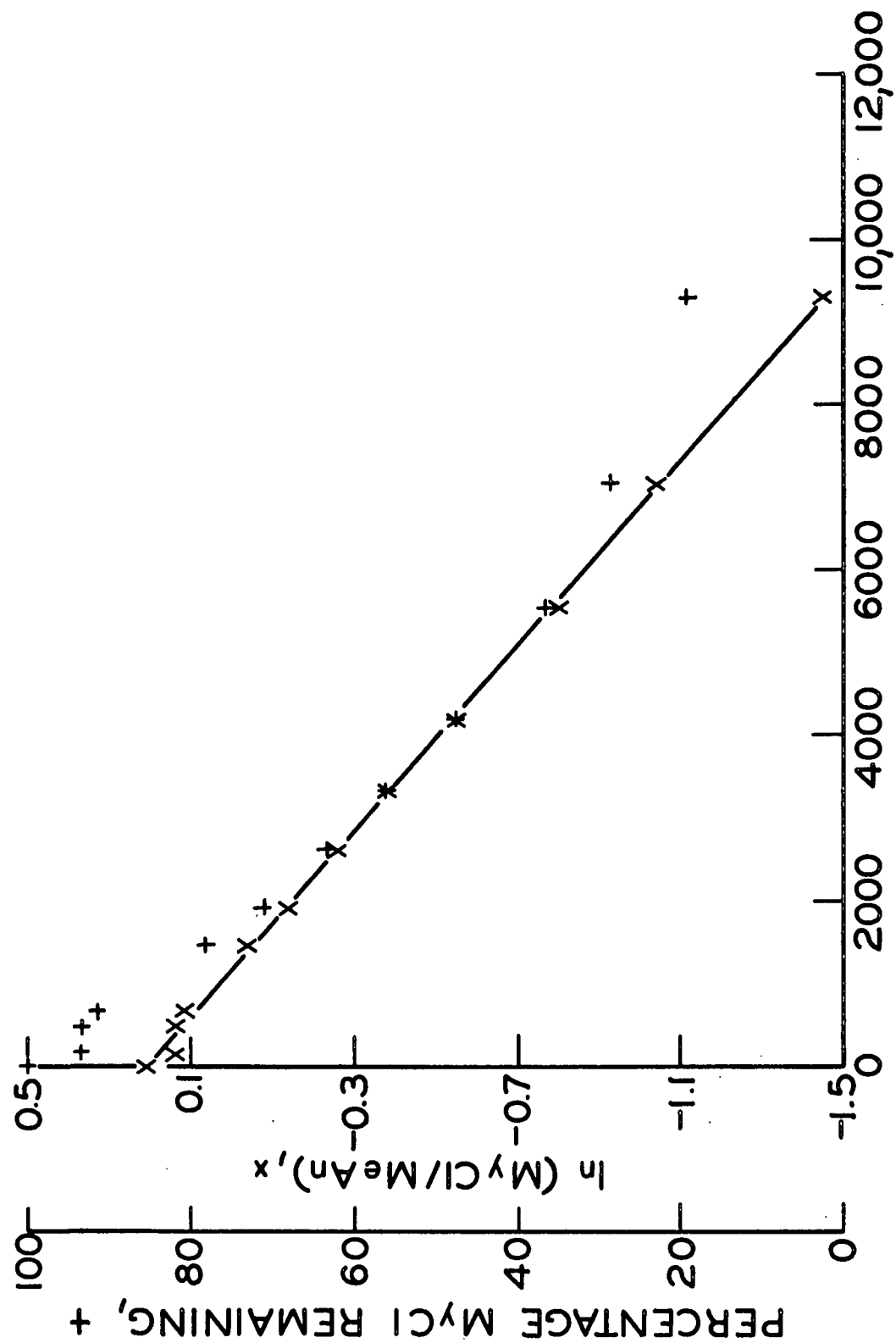

Figure 7. Plot of Percentage Myrtenyl Chloride Remaining, +, and ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(2.98 \pm 0.03) \times 10^{-6}$ sec.$^{-1}$. This Reaction was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 122

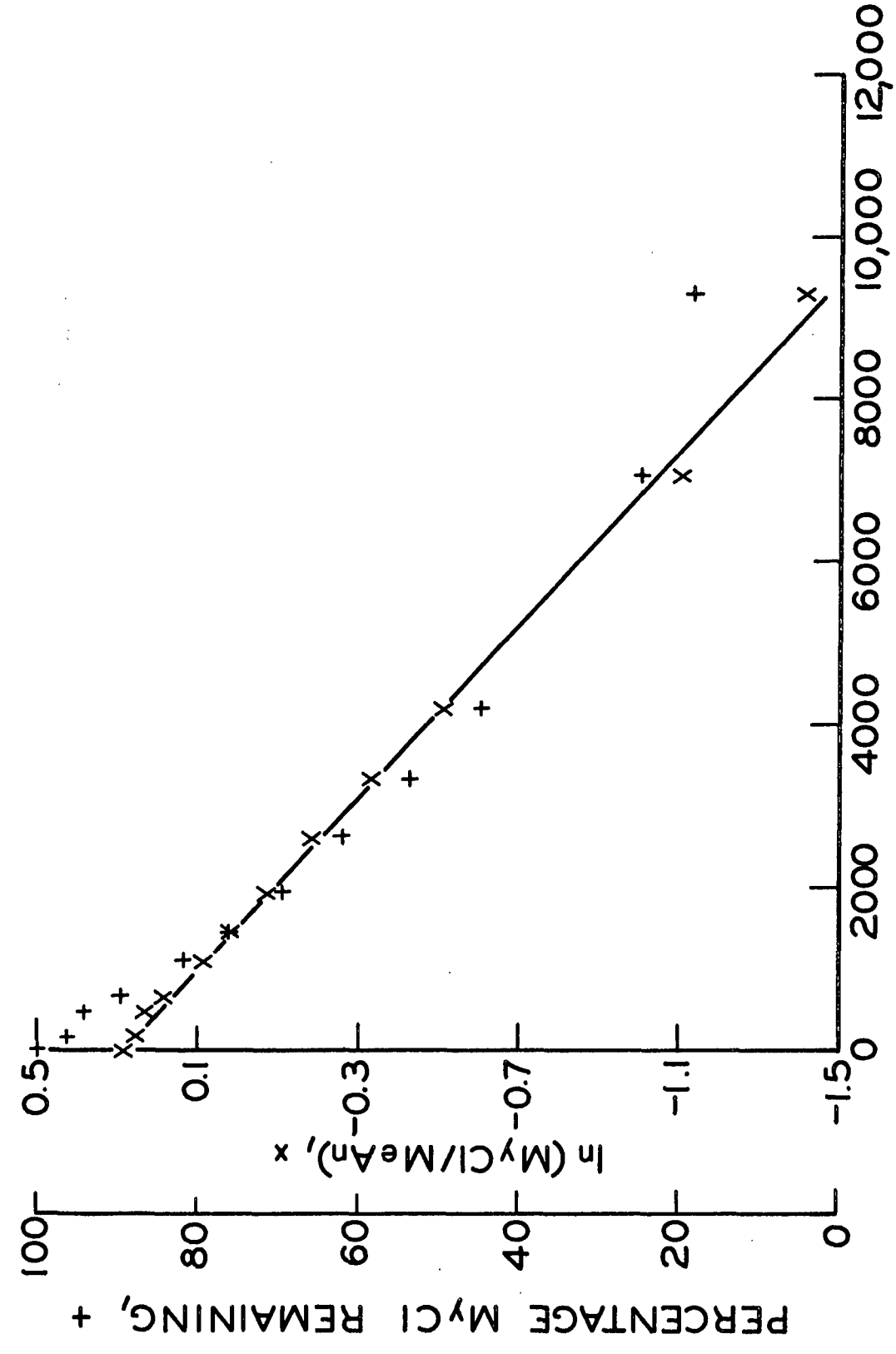

Figure 8. Plot of Percentage Myrtenyl Chloride Remaining, +, and ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, (3.14 ± 0.05) x 10^{-6} $sec.^{-1}$. This Reaction was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 124

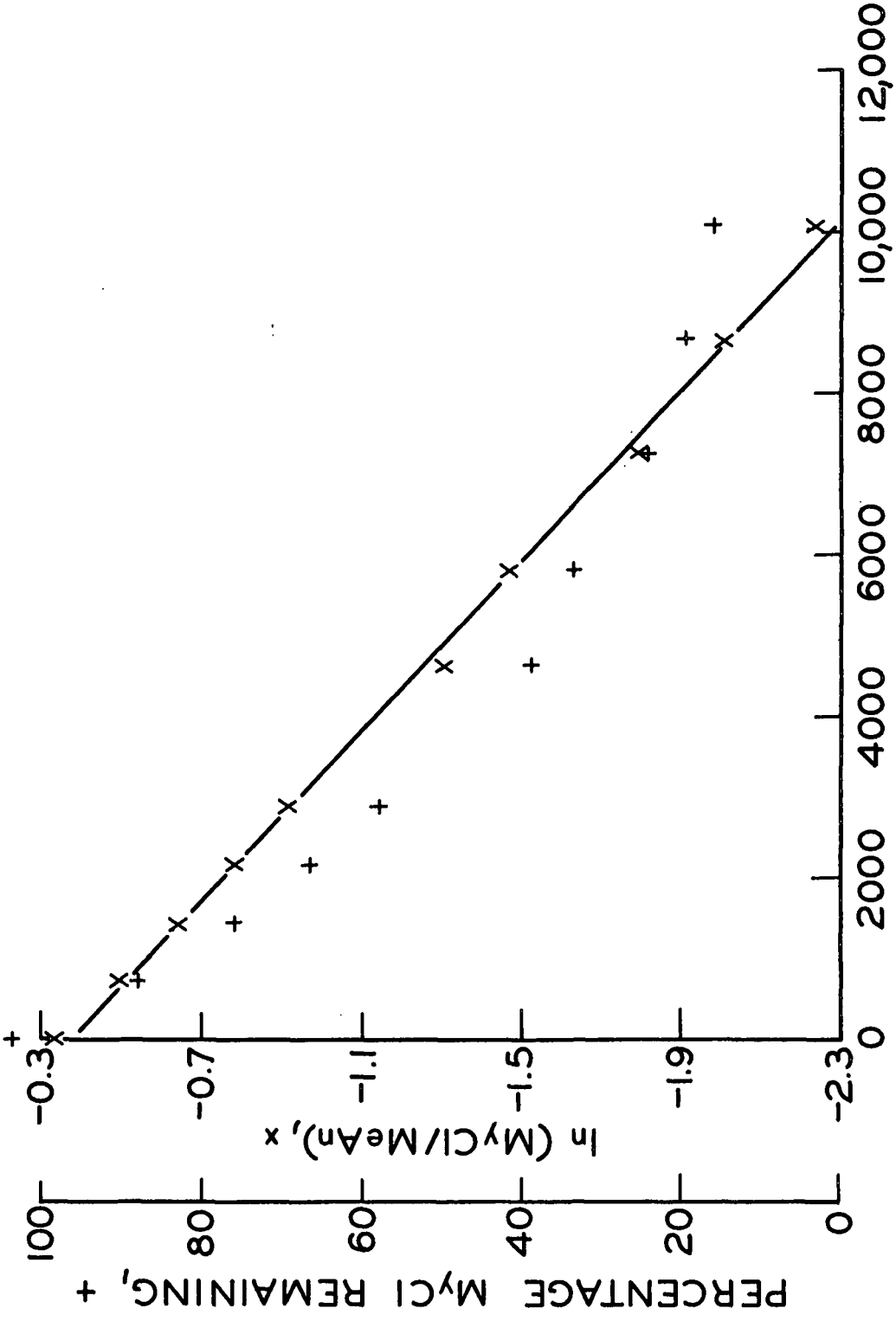

Figure 9. Plot of Percentage Myrtenyl Chloride Remaining, +, and ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(3.17 \pm 0.06) \times 10^{-6}$ sec.$^{-1}$. Lithium Perchlorate was 0.05M. This Run was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 90

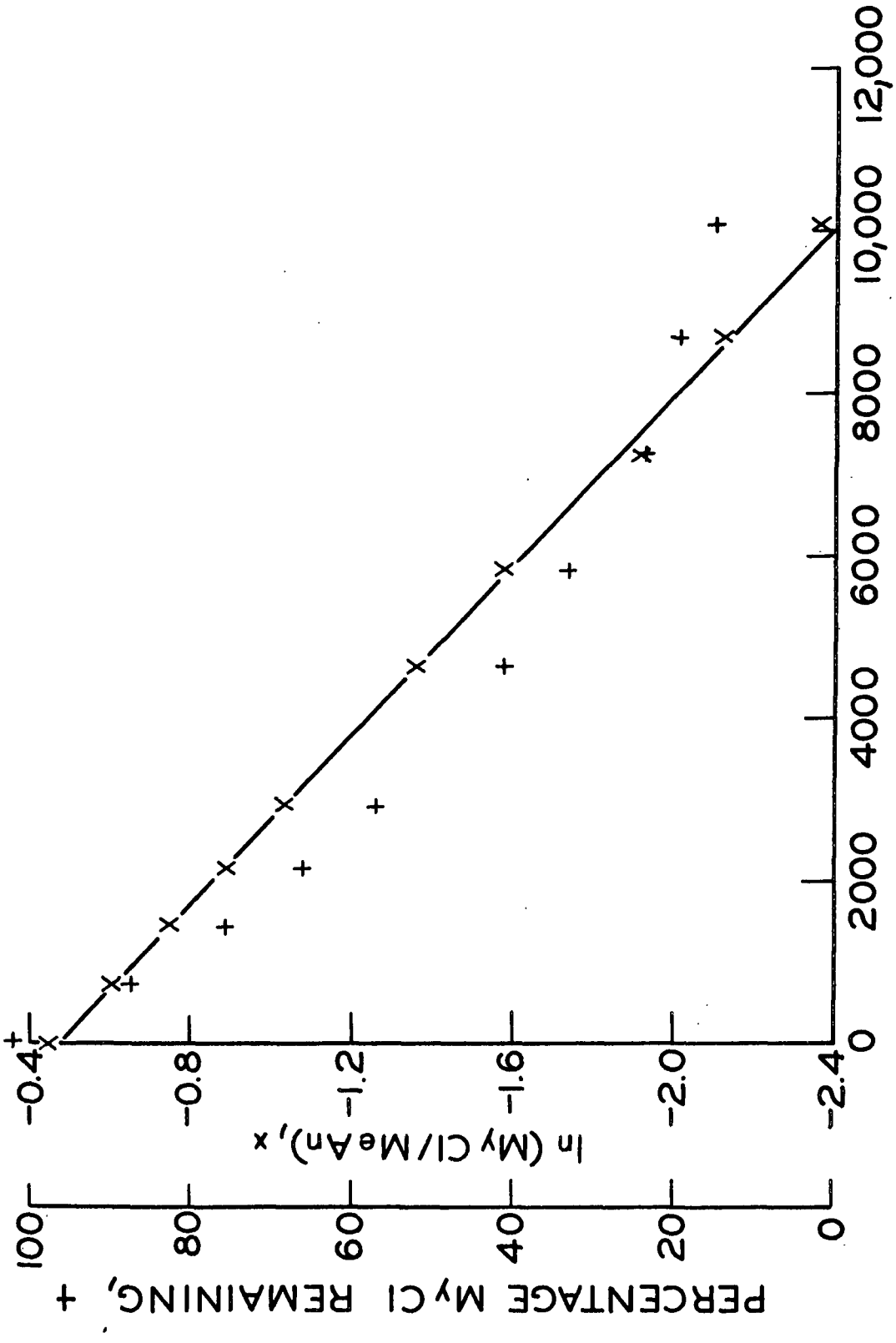

Figure 10. Plot of Percentage Myrtenyl Chloride Remaining, +, and of ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(3.19 \pm 0.04) \times 10^{-6}$ sec.$^{-1}$. Lithium Perchlorate was 0.05M. This Run was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 90

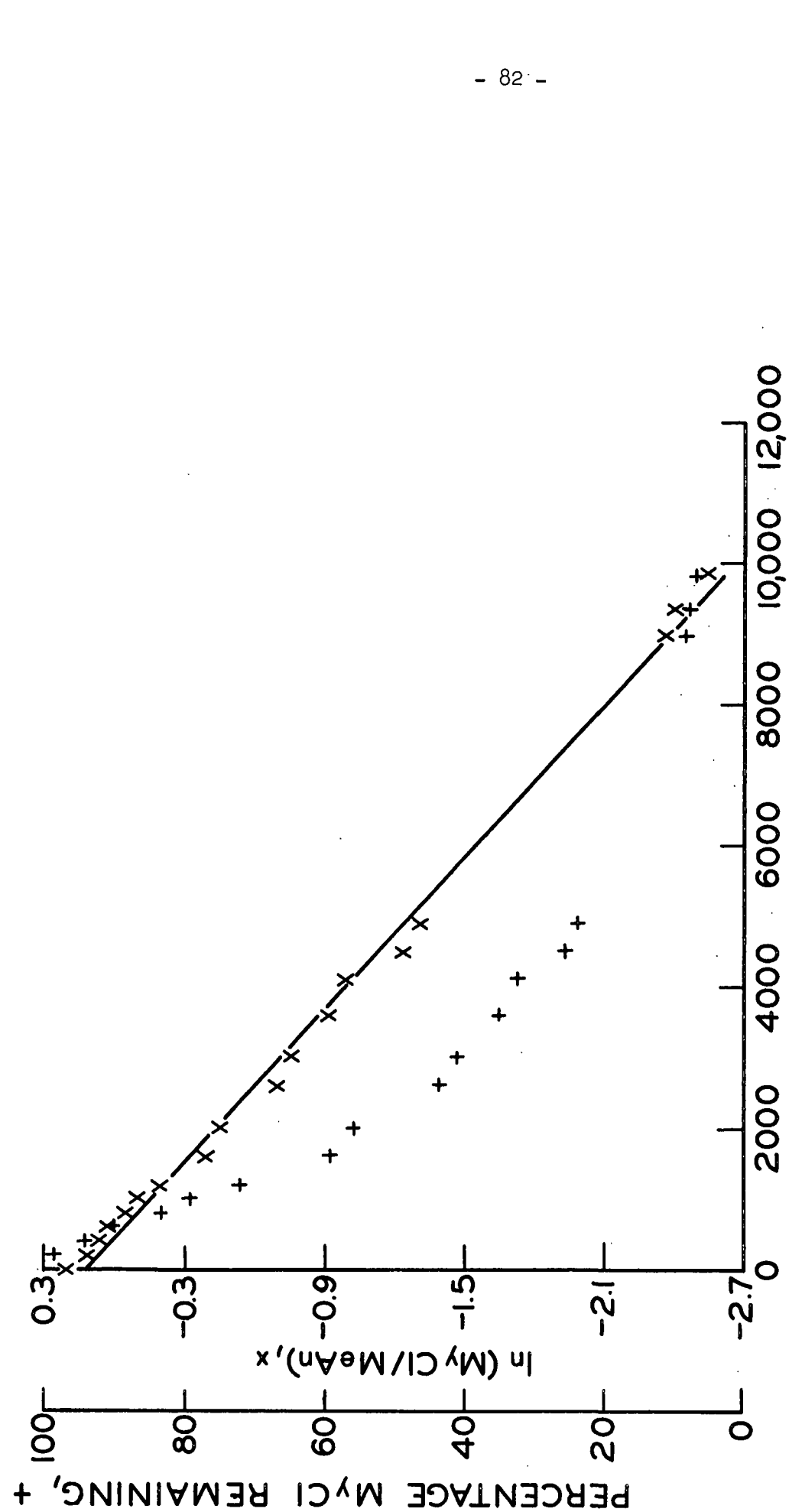

Figure 11. Plot of Percentage Myrtenyl Chloride Remaining, +, and of ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, (4.65 ± 0.08) x 10^{-6} $sec.^{-1}$. Initial Sodium Methoxide Concentration was 0.02M. Total Salt Concentration was Maintained at 0.05M Throughout the Series of Methoxide Runs by Addition of Lithium Perchlorate. Temperature was 35.0°C. Run 76

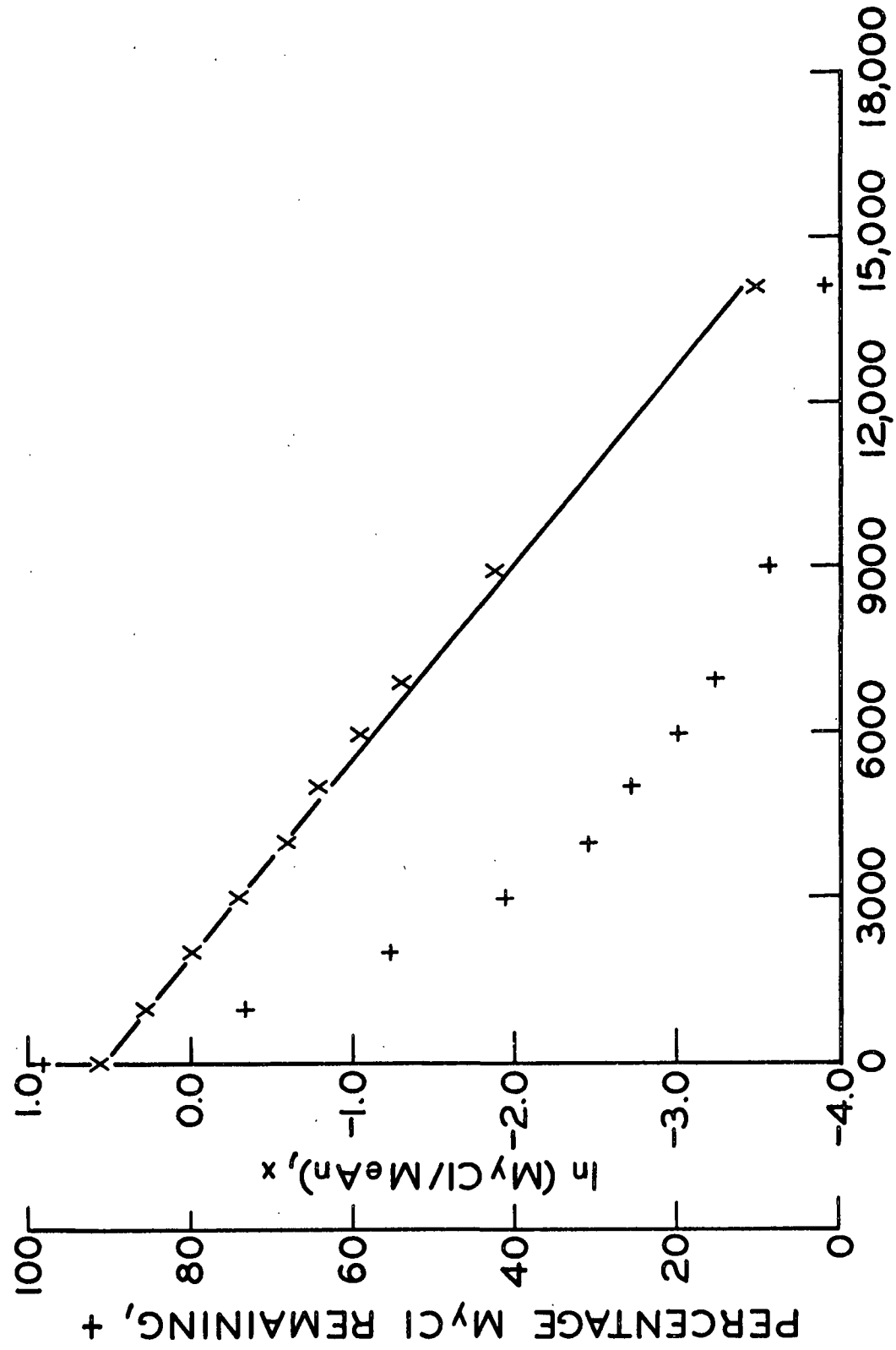

Figure 12. Plot of Percentage Myrtenyl Chloride Remaining, +, and of ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(4.68 \pm 0.09) \times 10^{-6}$ sec.$^{-1}$. Initial Sodium Methoxide Concentration was 0.02M. Total Salt Concentration was Maintained at 0.05M Throughout the Series of Methoxide Runs by Addition of Lithium Perchlorate. Temperature was 35.0°C. Run 76

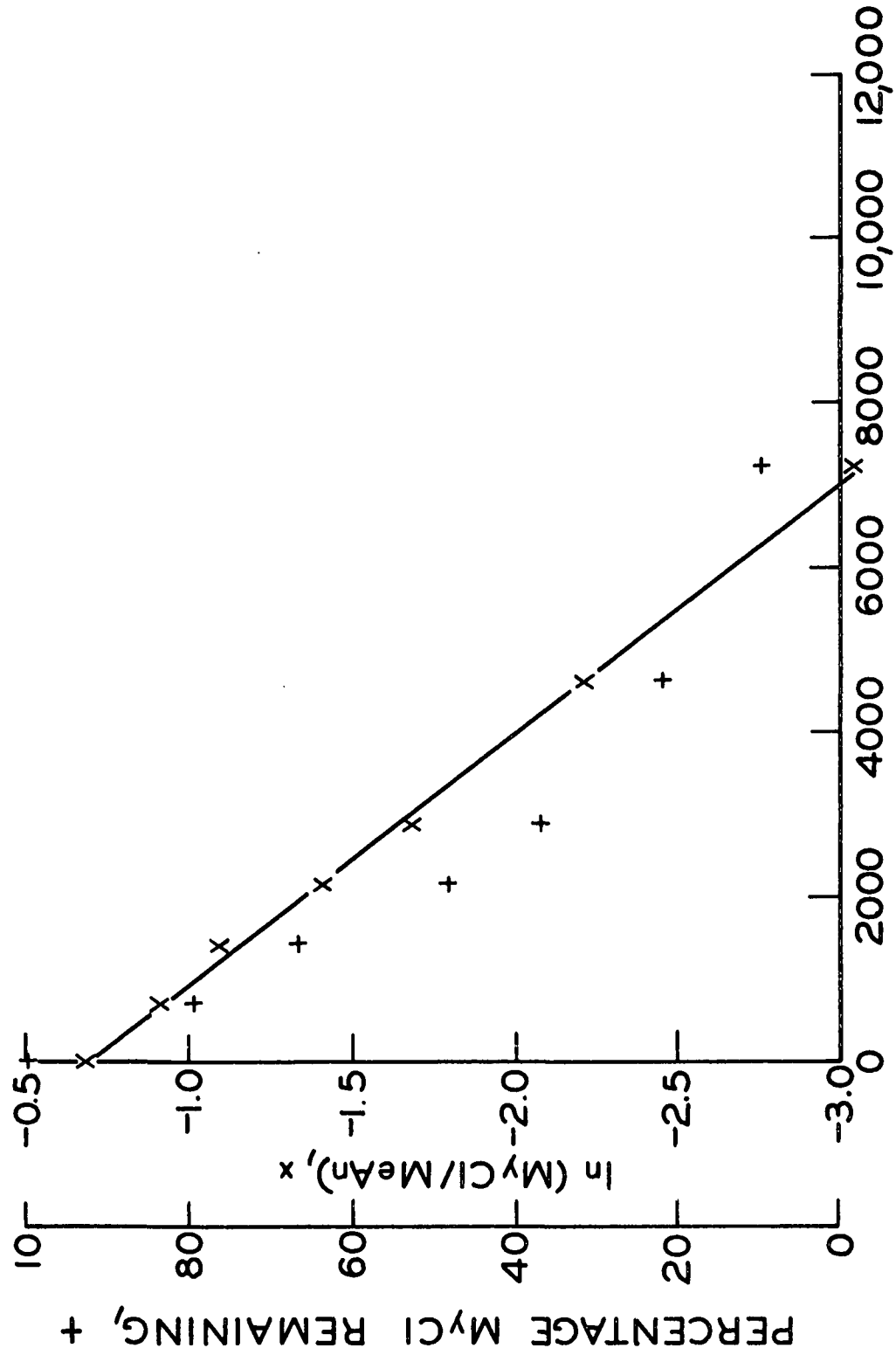

Figure 13. Plot of Percentage Myrtenyl Chloride Remaining, +, and of ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(5.48 \pm 0.11) \times 10^{-6}$ sec.$^{-1}$. Initial Sodium Methoxide Concentration was 0.035M. Total Salt Concentration was Maintained at 0.05M Throughout the Series of Methoxide Runs by Addition of Lithium Perchlorate. Temperature was 35.0°C. Run 94

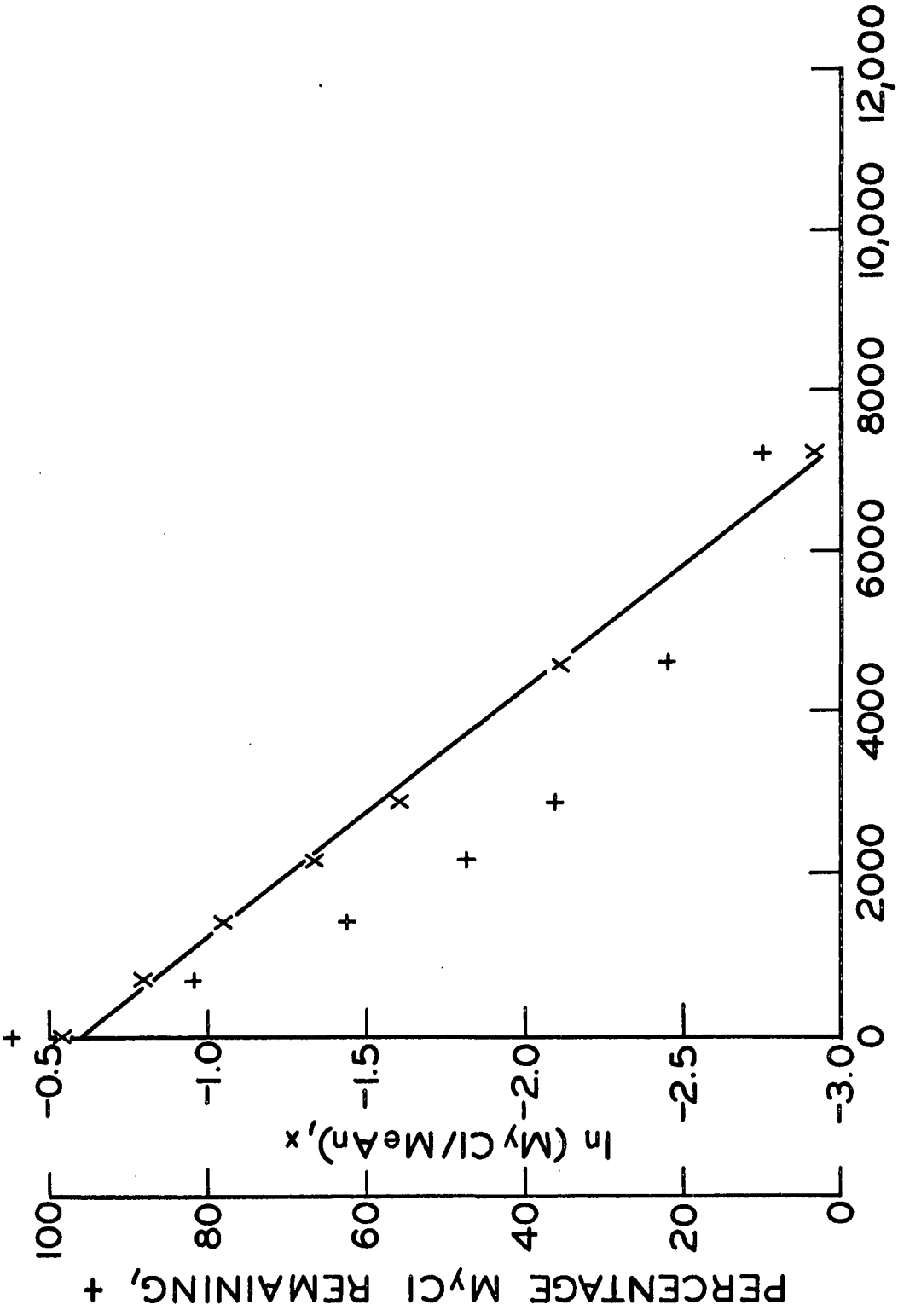

Figure 14. Plot of Percentage Myrtenyl Chloride Remaining, +, and of ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(5.48 \pm 0.13) \times 10^{-6}$ sec.$^{-1}$. Initial Sodium Methoxide Concentration was 0.035M. Total Salt Concentration was Maintained at 0.05M Throughout the Series of Methoxide Runs by Addition of Lithium Perchlorate. Temperature was 35.0°C. Run 96

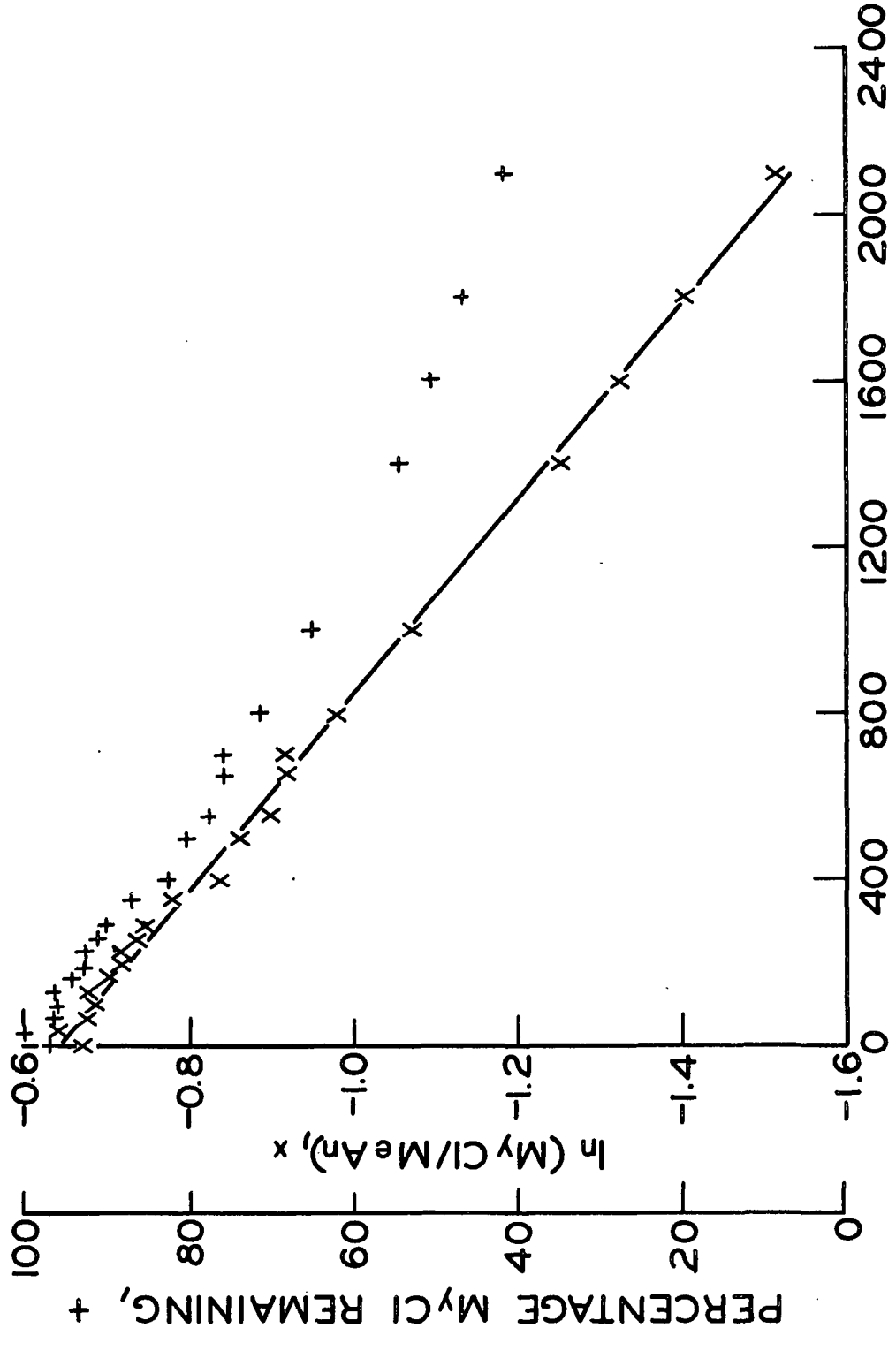

Figure 15. Plot of Percentage Myrtenyl Chloride Remaining, +, and of ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(7.06 \pm 0.09) \times 10^{-6}$ sec.$^{-1}$. Initial Sodium Methoxide Concentration was 0.05M. Temperature was 35.0°C. Run 72

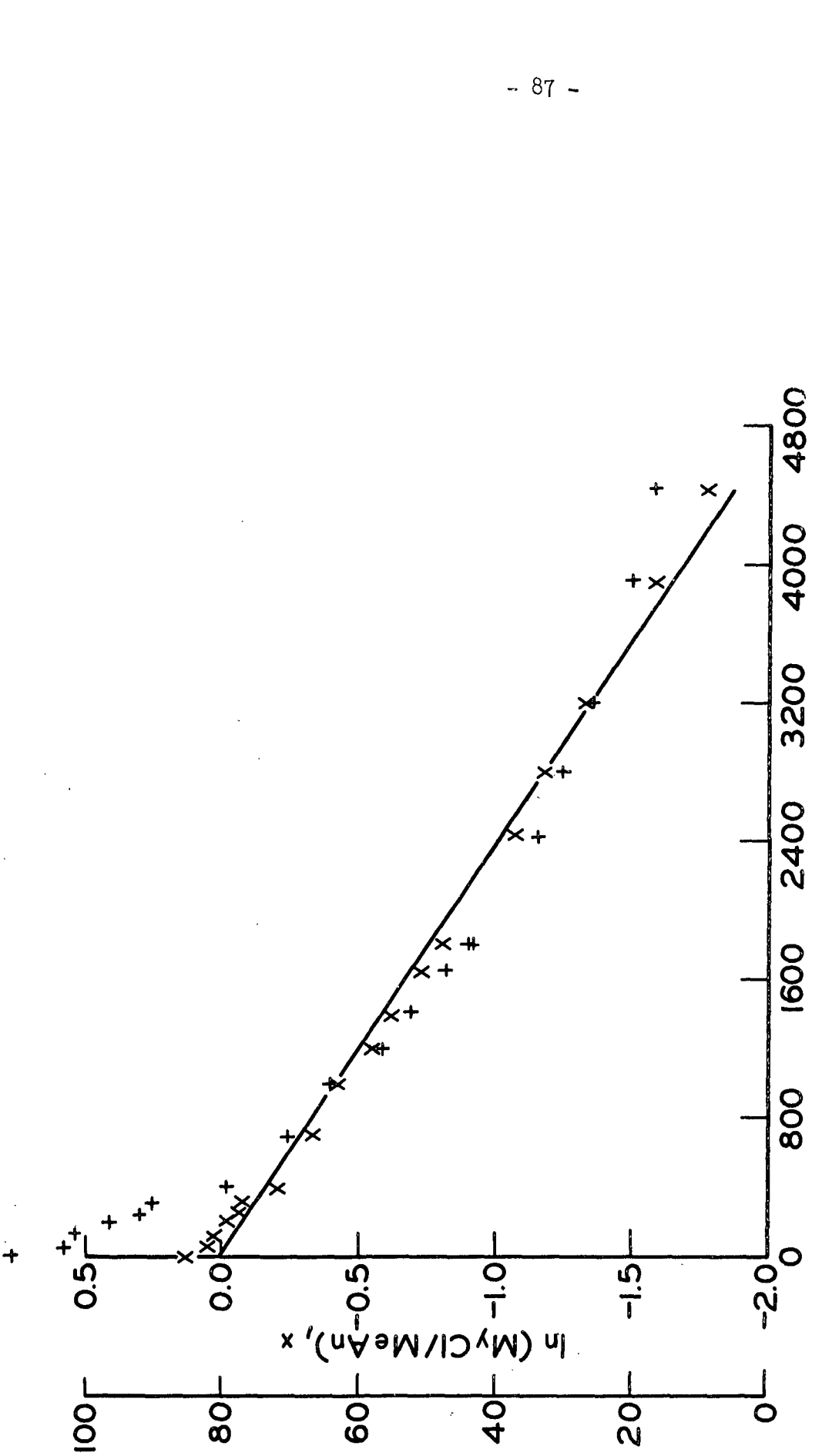

Figure 16. Plot of Percentage Myrtenyl Chloride Remaining, +, and of ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. Rate Constant is the Slope, $(7.09 \pm 0.17) \times 10^{-6}$ sec.$^{-1}$. Initial Sodium Methoxide Concentration was 0.05M. Temperature was 35.0°C. Run 73

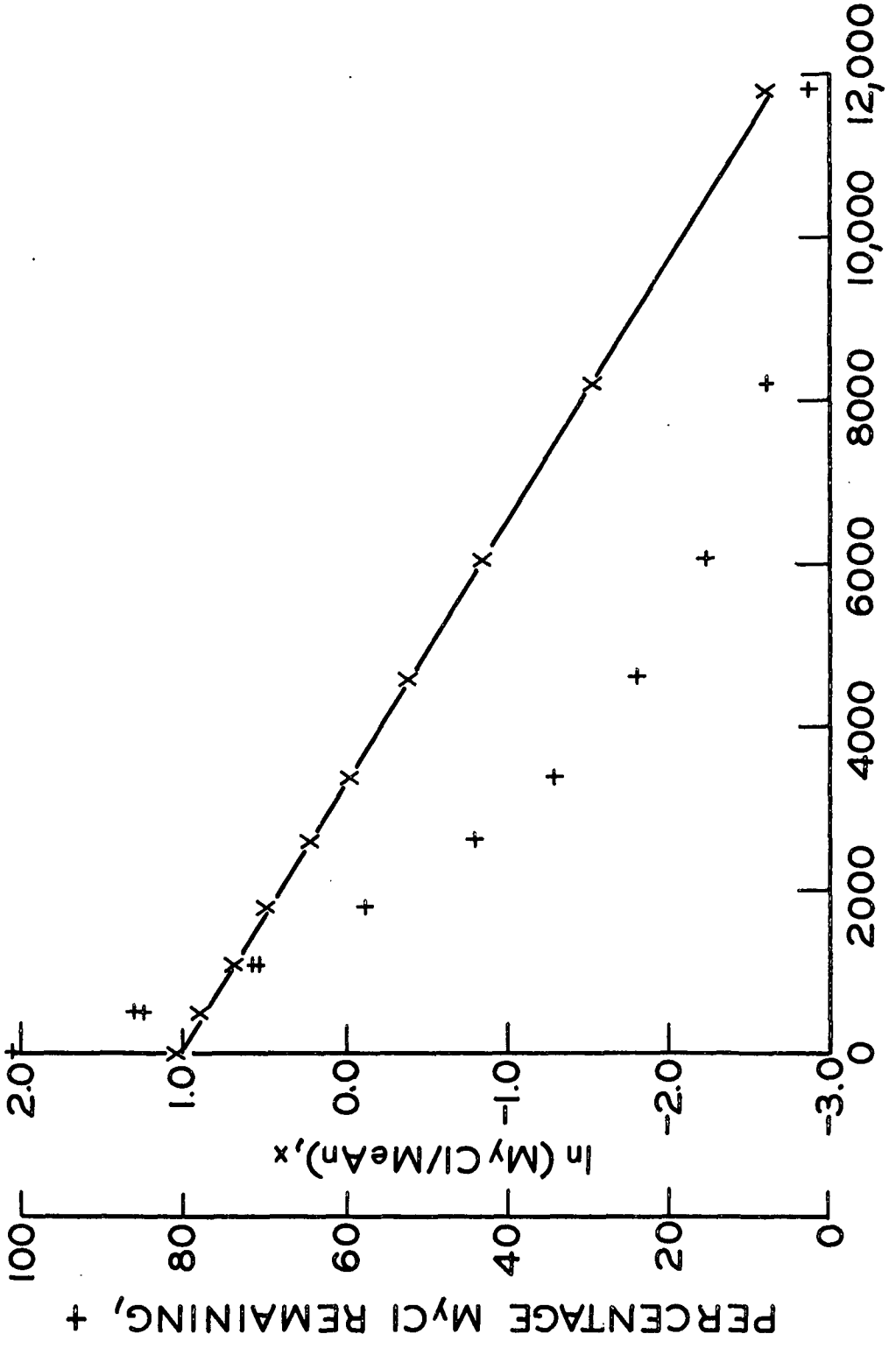

Figure 17. Plot of Percentage Myrtenyl Chloride Remaining, +, and of ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, (5.19 ± 0.02) x 10^{-6} $sec.^{-1}$. Initial Potassium Acetate Concentration was 0.3M. Temperature was 35.0°C. Run 140

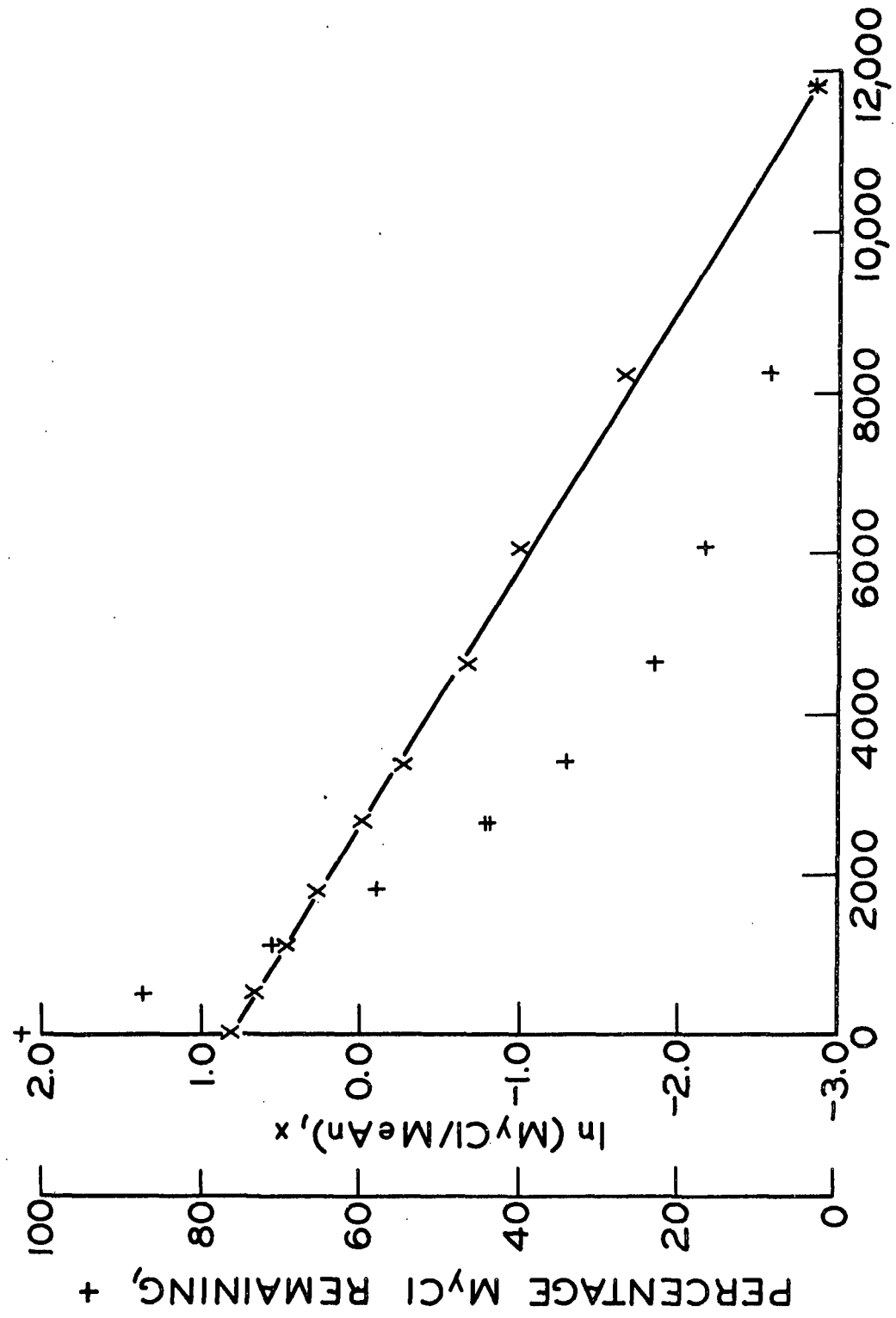

Figure 18. Plot of Percentage Myrtenyl Chloride Remaining, +, and of ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(5.14 \pm 0.05) \times 10^{-6}$ sec.$^{-1}$. Initial Potassium Acetate Concentration was 0.3M. Temperature was 35.0°C. Run 142

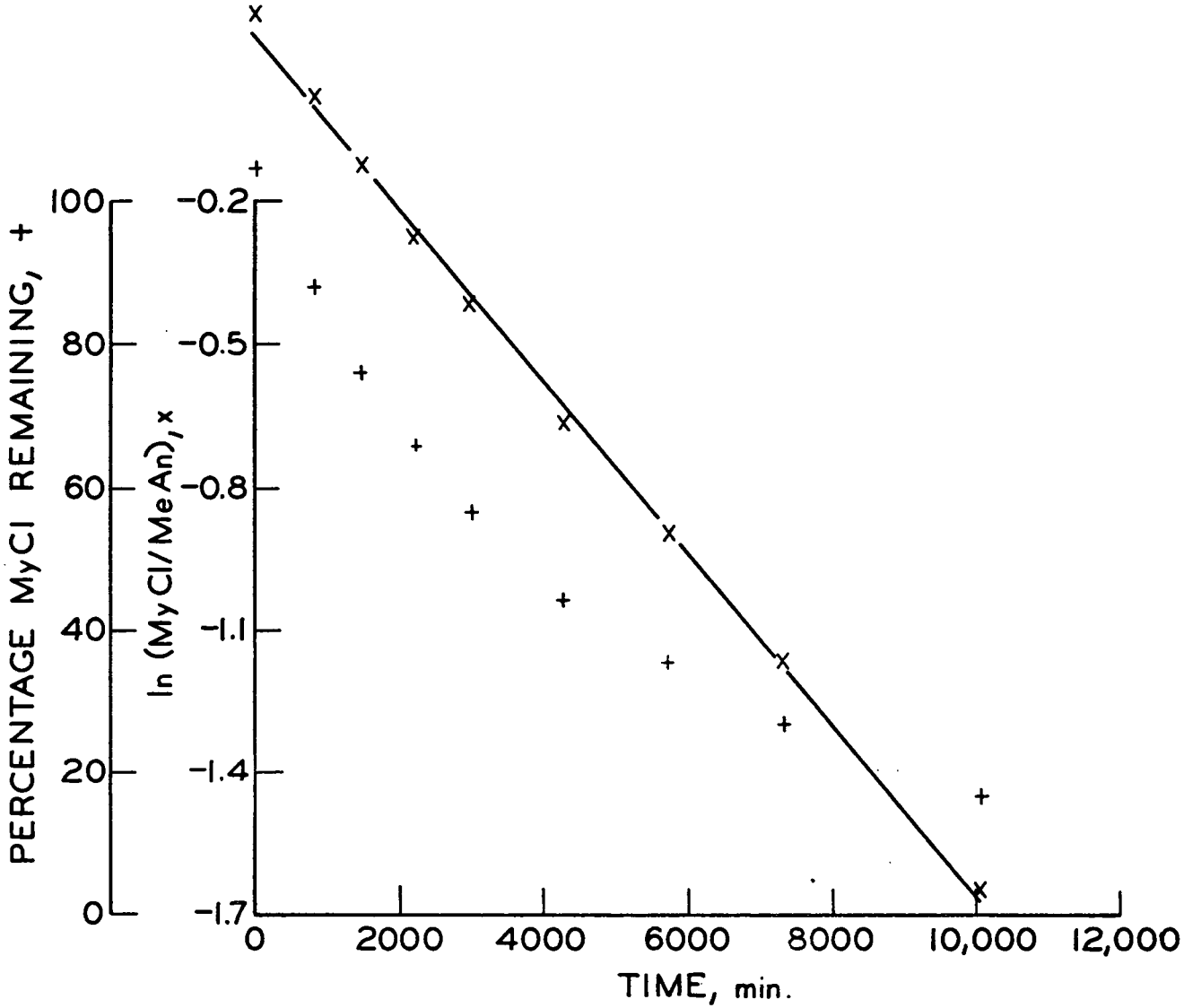

Figure 19. Plot of Percentage Myrtenyl Chloride Remaining, +, and ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(3.02 \pm 0.05) \times 10^{-6}$ sec.$^{-1}$. Lithium Chloride was 0.05M. This Run was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 102

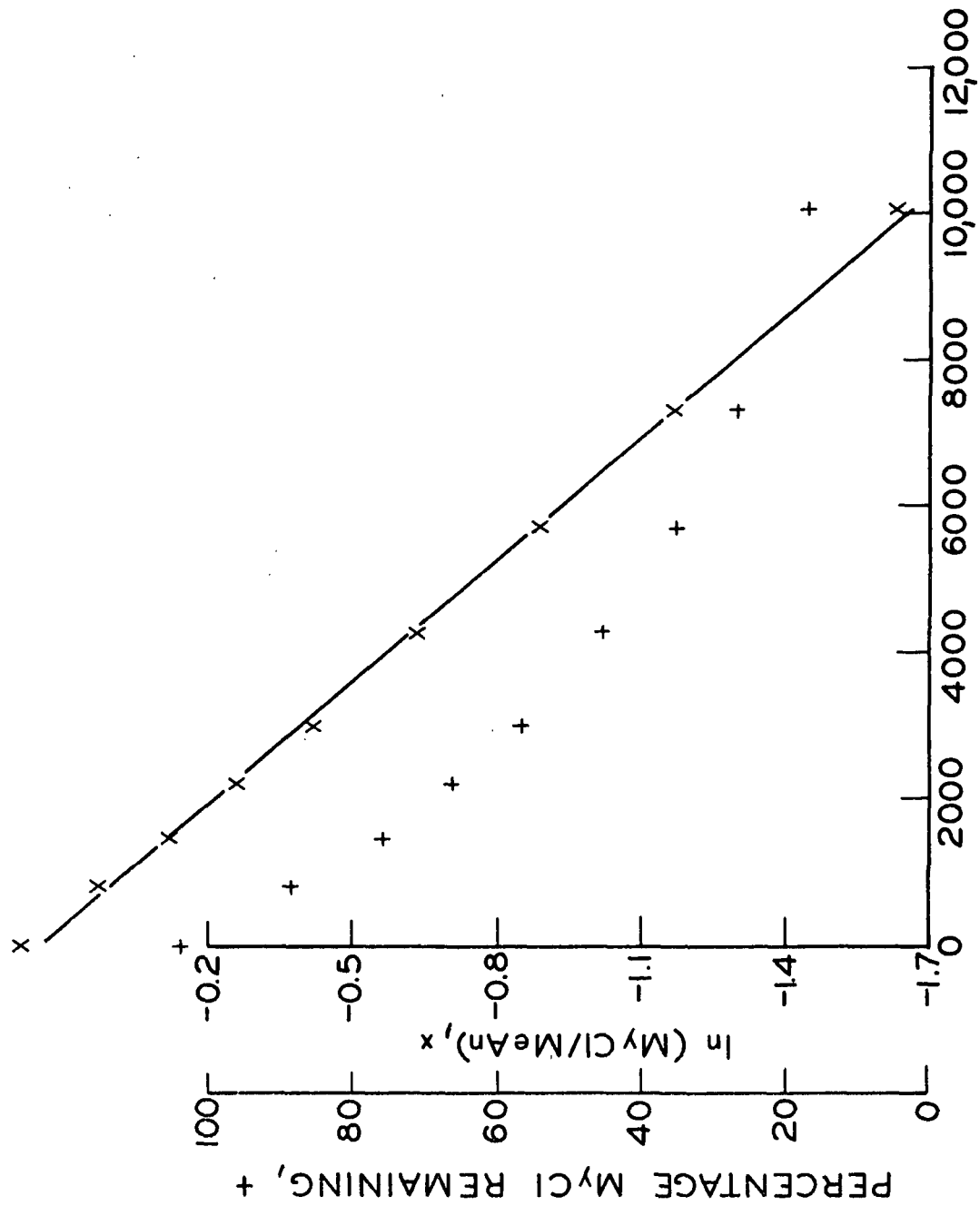

Figure 20. Plot of Percentage Myrtenyl Chloride Remaining, +, and ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(3.01 \pm 0.05) \times 10^{-6}$ sec.$^{-1}$. Lithium Chloride was 0.05M. This Run was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 104

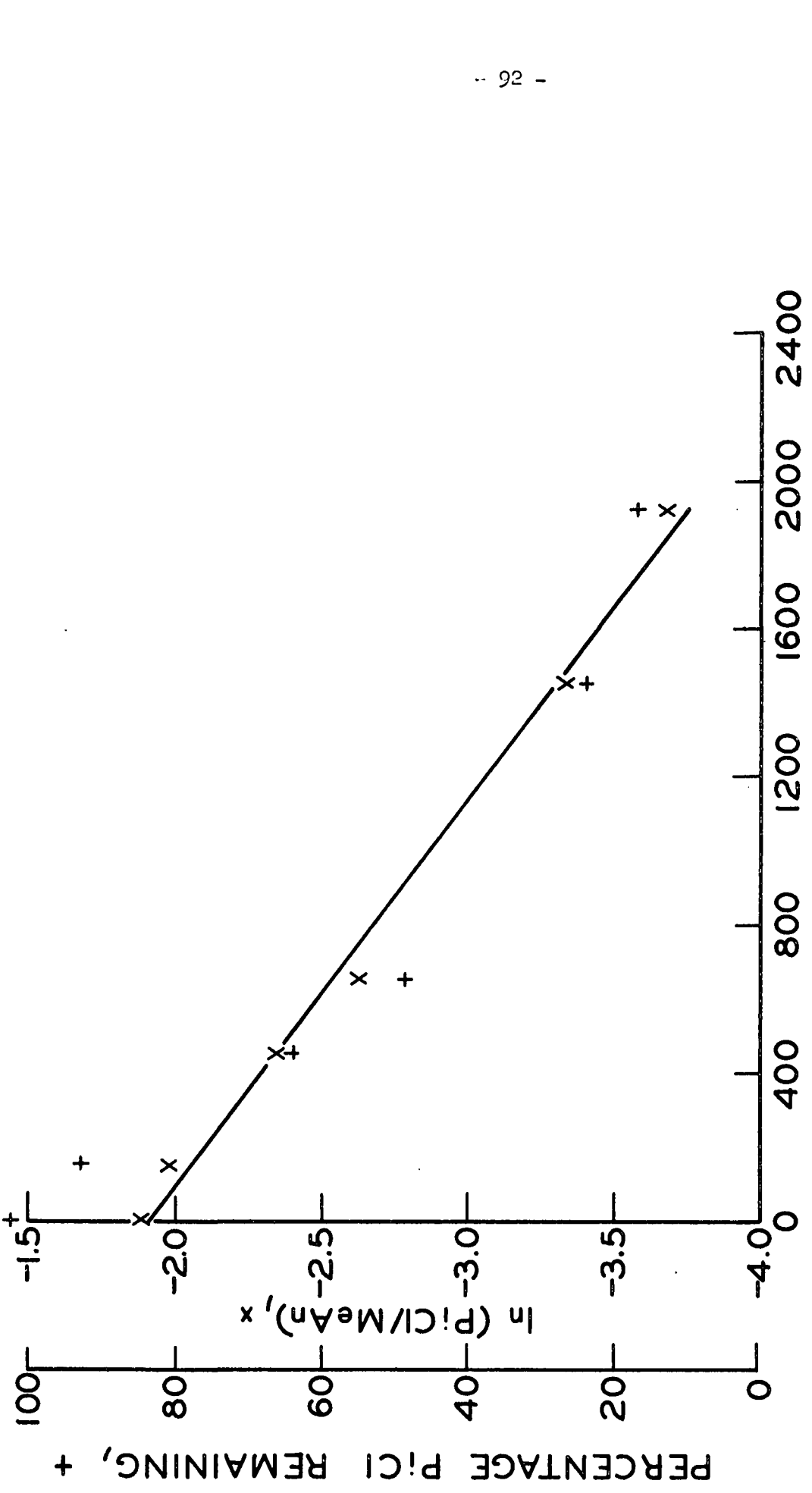

Figure 21. Plot of Percentage trans-Pinocarvyl Chloride Remaining, +, and of ln(PiCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(PiCl/MeAn) on Time. The Rate Constant is the Slope, $(16.0 \pm 0.7) \times 10^{-6}$ sec.$^{-1}$. GLC was Done on the ODPN Column. This Run was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 122

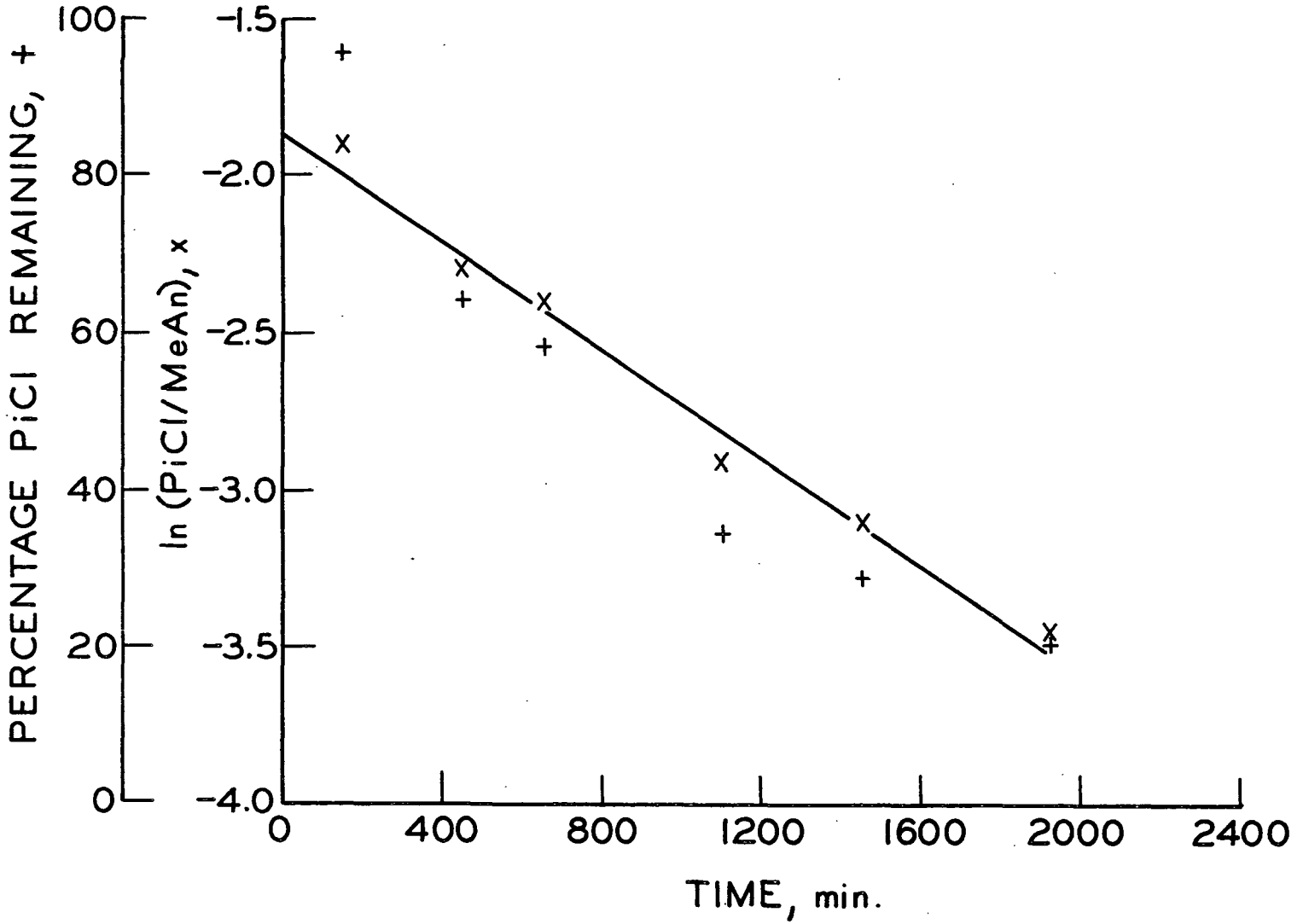

Figure 22. Plot of Percentage trans-Pinocarvyl Chloride Remaining, +, and of ln(PiCl/MeAn), x, vs. Time. The Solid Line is the Regression of ln(PiCl/MeAn) on Time. The Rate Constant is the Slope, $(14.3 \pm 0.9) \times 10^{-6}$ sec.$^{-1}$. This Run was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 124

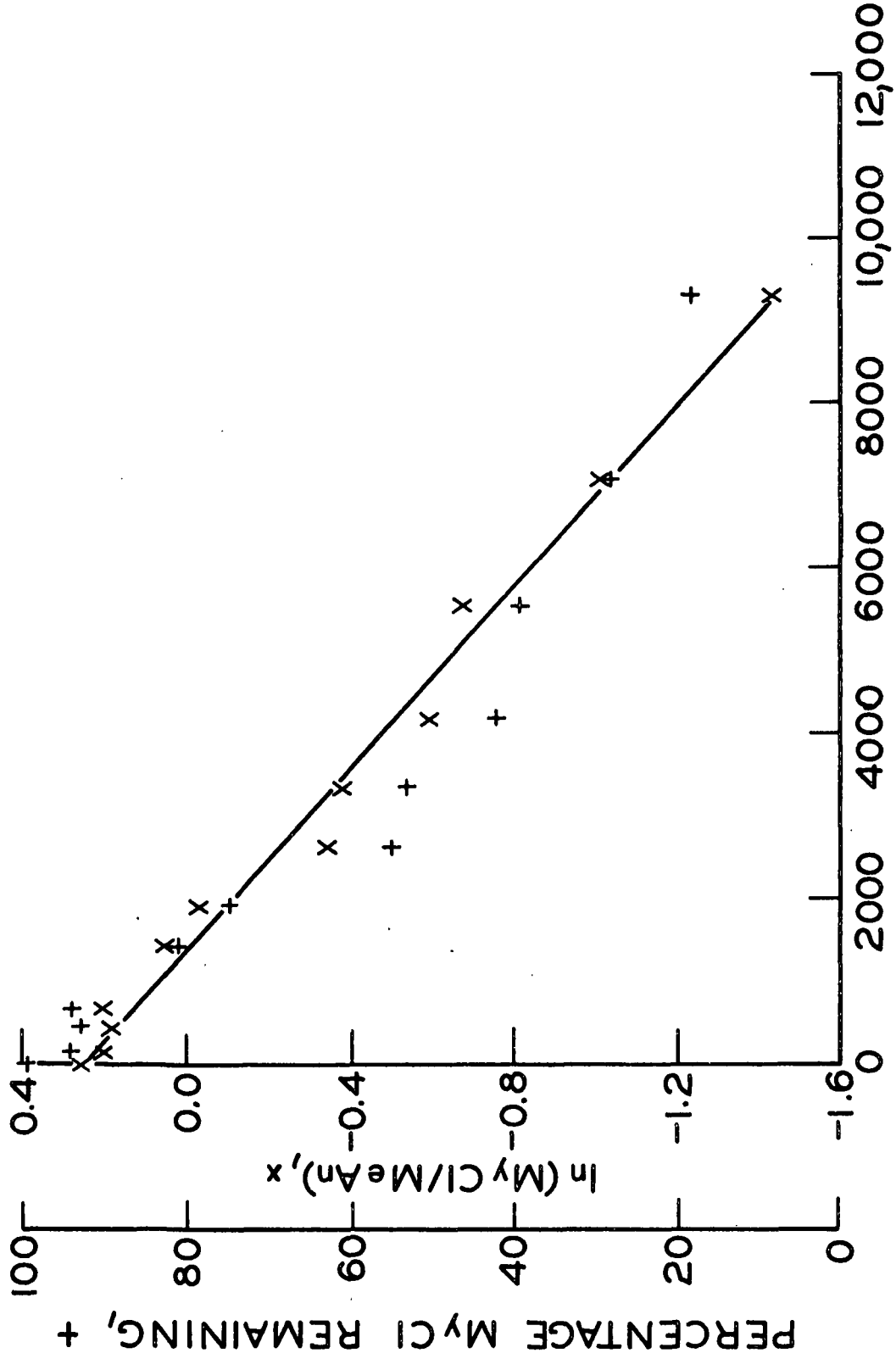

Figure 23. Plot of Percentage Myrtenyl Chloride Remaining, +, and of ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(3.05 \pm 0.11) \times 10^{-6}$ sec.$^{-1}$. GLC was Done on the ODPN Column. This Run was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 122

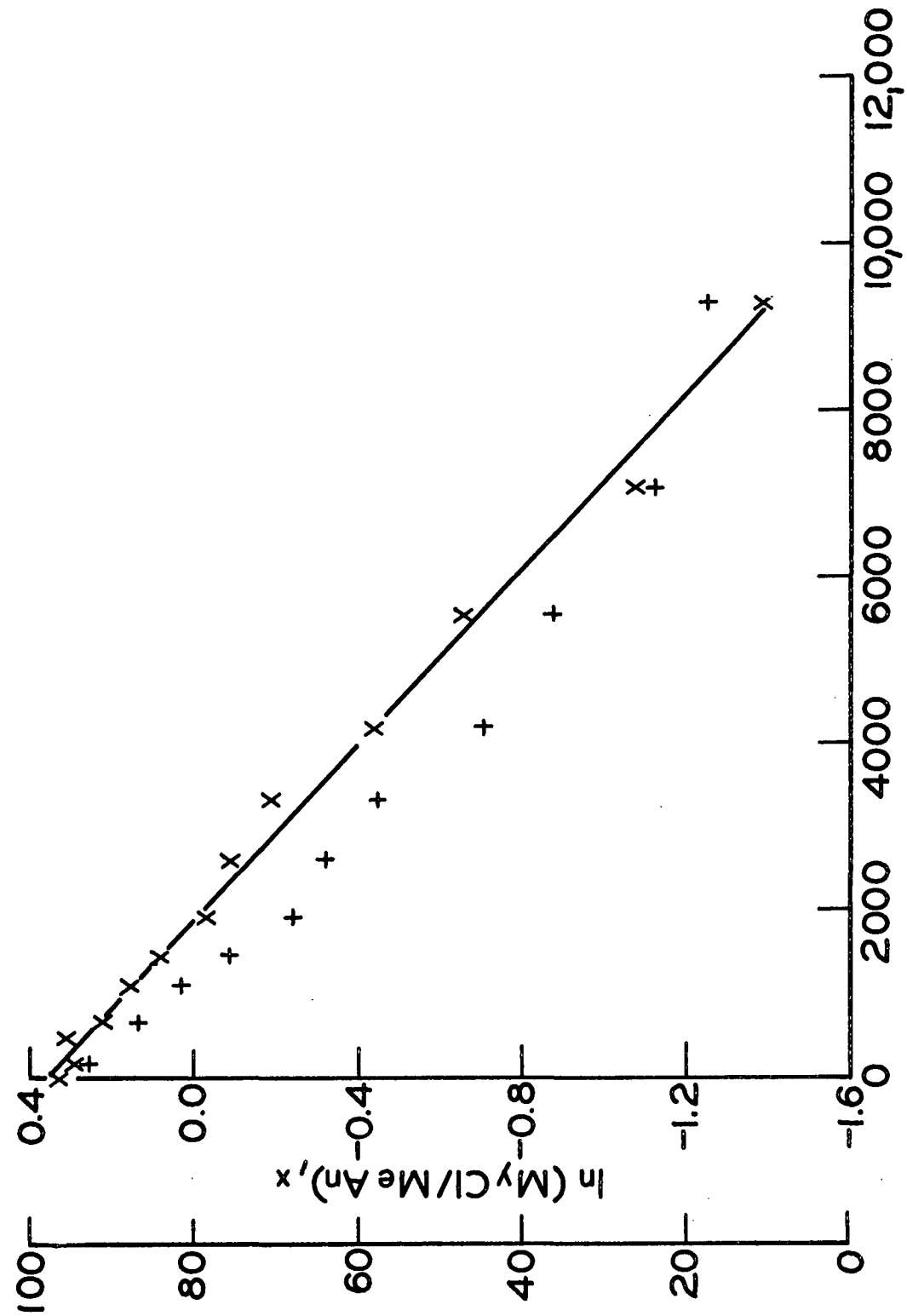

Figure 24. Plot of Percentage Myrtenyl Chloride Remaining, +, and of ln(MyCl/MeAn), x, vs. Time. The Solid Line is the Regression ln(MyCl/MeAn) on Time. The Rate Constant is the Slope, $(3.17 \pm 0.08) \times 10^{-6}$ sec.$^{-1}$. GLC was Done on the ODPN Column. This Run was Buffered with 2,6-Dimethylpyridine. Temperature was 35.0°C. Run 124